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c — correspondence	MMS — Massachusetts Med cal Soc city	mr — meeting report	o — obituary
cr — case record	mp — medical progress	m sc — miscellaneous	* — original article
e — editorial	me — medical eponym	n — notice	

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SUBDIAPHRAGMATIC ABSCESS IN CHILDREN*

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BOSTON

A RECENT experience with the problem presented by a subdiaphragmatic abscess complicating the postoperative course of a three-year-old boy with a ruptured appendix has led us to review the cases previously seen at the Children's Hospital with this condition. As a late complication of intra-abdominal sepsis in children, subphrenic abscess ranks as a rare but important offender. It may occasionally occur as the only site of intra-abdominal infection, in which case its recognition may be difficult. It is generally agreed that the mortality of untreated subdiaphragmatic abscess is between 90 and 100 per cent. Clearly early diagnosis and rational treatment are imperative under such threatening circumstances. Fourteen patients have been seen at the Children's and Infants' hospitals in whom an abscess in the subdiaphragmatic space has been recognized. Eleven of these were treated surgically, with 1 death; the other 3 had cases of fulminating infection and died, and at post mortem a subphrenic abscess was found as one among multiple manifestations of generalized sepsis.

INCIDENCE

Subphrenic abscess is encountered less frequently in infants and children than in adults. Thus, in Gatewood's¹ 41 cases, only 1 patient was a child, aged eight. Brown² reports 4 patients under ten years. Ireland³ presents 6 patients under twelve. In the cases, both collected and personal, presented by Ochsner and DeBakey⁴ the youngest age group considered was from nine to nineteen. Apparently none of their patients were younger than nine.

The present series comprises 14 patients under eleven years of age, 6 of whom were less than two years old. There were 9 boys and 5 girls. All but one of the patients were of the white race.

The incidence of subphrenic abscess as a complication of acute appendicitis is not high, even though one of the most frequent causes of all subphrenic abscesses is a suppurative lesion of the appendix. In 15,000 collected cases⁴ of acute appendicitis, approximately 0.9 per cent suffered this complication. The incidence in children seems to be even lower. At the Children's Hospital in recent years, 860 children with acute appendicitis have been seen; 3 patients subsequently developed subphrenic abscess, an incidence of roughly 0.3 per cent.

PATHOGENESIS

The mode of infection of the subphrenic spaces in our series (Table 1) is quite varied, and sug-

TABLE 1. *Mode of Infection in Subdiaphragmatic Abscess.*

PATHOGENESIS	NO. OF CASES
Following intra abdominal sepsis	9
Ruptured appendix	5
Primary peritonitis	1
Rupture of ileum	1
Liver abscess	2
Metastatic from a distant focus	4
Upper respiratory infection	2
Otitis media	1
Hordeola	1
Traumatic	1
Total	14

gests that several different mechanisms may be at work in the introduction of infection into those regions.

In the experience of all observers a suppurative appendix is the commonest preceding event. This was true in our series, with 5 patients (36 per cent) falling into this category. It has been thought by many that the course of the infection is by direct extension up the right gutter. If this were true, one would expect the right posterosuperior space to be most frequently involved, as is indeed the case in the large collected series of Ochsner and

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lead to a more rational operative approach. However, in children this is less readily done than in older patients. In the child, the signs of the underlying infection may extend so widely that they overlap anatomic regions, thus leaving the examiner in some doubt concerning the exact space primarily involved.

In this series, the abscesses were localized as follows: right anterosuperior, 8 cases; right posterior, 3 cases; and right inferior, left superior and left anteroinferior, 2 cases each. It will be seen that the right anterosuperior space was by far the most frequently involved space. This is in distinct contrast to the published incidence of a large series of collected cases,⁴ where the right posterosuperior space was most commonly involved. For this, we have no anatomical or etiologic explanation.

CLINICAL ASPECTS

The symptomatology of subdiaphragmatic abscess as presented by our patients has shown considerable variation, but it appears that, in children at least three different types of clinical picture are encountered. These roughly parallel the different modes of origin of the infection as discussed above.

The first group comprise those cases in which the subphrenic infection is merely part of a wide spread intra-abdominal suppurative process. In these patients there is a rather abrupt onset of what appears to be a severe infectious disease. The constitutional signs of fever, anorexia, prostration, malaise and tachycardia are associated with some evidence of intra-abdominal involvement, such as vomiting, abdominal pain, diarrhea, tenderness, spasm and decrease or absence of intestinal peristalsis. The course of the disease tends to be fulminating, the patient dying within a few days from the onset. In 3 of our patients, this type of course was observed. One had a primary peritonitis associated with empyema and septicemia, another had peritonitis secondary to a ruptured ileum (above an atresia), and the third had a septic thrombophlebitis of the umbilical vein with peritonitis, multiple liver abscesses, bronchopneumonia and septicemia. In all these patients, the small subphrenic abscesses found post mortem represented but a minor and relatively insignificant part of a fulminating generalized sepsis. None were recognized clinically before death, but such recognition could have in no way altered their course.

The second group, wherein the subphrenic infection complicates the course of acute ruptured appendicitis, is the type most commonly seen. The clinical syndrome has been thoroughly described in the literature, and the progress of the

infection in children seems to differ in no significant way from that observed in adults. The persistence of the evidences of infection as demonstrated by continued fever and tachycardia, malaise and elevation in the number of leukocytes, which is unexplained by the abdominal, rectal or urinary findings or by the condition of the wound, suggests the walling off of an infectious process in some other area. The localizing signs in our experience have been varied. Tenderness along the course of the twelfth rib or over the liver is usually present. We have, however, been unable to distinguish between anterior-space and posterior-space infections by this means. Spasm in the right upper quadrant of the abdomen, or even a palpable mass, is frequently present. Pleural effusion, as suggested by dullness or flatness to percussion, diminution in tactile fremitus and distant breath sounds, is usually found. Indeed, the problem most commonly resolves itself into a differential diagnosis between a subphrenic infection and a pulmonary complication. In this distinction the roentgenologic findings are of considerable importance. In our series the most consistent signs observed were elevation and fixation of the diaphragm. These findings have been emphasized by Granger,⁸ Lewald,⁹ Pancoast¹⁰ and others. In 2 patients only was air observed beneath the diaphragm. Thus, when present, gas is of diagnostic significance, but it is usually not present or is a late finding, and hence its absence is of no significance. Obliteration of the costophrenic angle with a diffuse haziness suggesting pleural effusion is frequently present. In 3 of our patients, however, the diaphragms were described as normal in position, contour and motion, and no fluid was observed in the pleural space. Thus, the roentgenologic examination may be of aid, but no observable abnormality may be present, and no commonly found variation from normal is pathognomonic.

The third group, perhaps the most interesting and difficult to diagnose, comprises those cases in which the subphrenic abscess is metastatic and is at once the chief or only disease present and the cause of the patient's admission to the hospital. These patients have a history of upper respiratory infection, otitis media or recurrent superficial staphylococcal infection. This is followed some days later by the vague and insidious onset of mild malaise and anorexia, associated with low-grade pyrexia. These symptoms persist, and there begin occasional attacks of abdominal pain. These rather mild symptoms gradually increase over a period of one to three months until the patient is finally brought to the hospital because of the appearance of a mass in the upper abdo-

DeBakey.⁴ In our few cases, however, the anterior space was more frequently involved than the posterior one following appendicitis, suggesting that some other mechanism may have been present. The possibility of lymphatic extension has been emphasized by Truesdale.⁵ We have routinely used Fowler's position in all patients with intra-abdominal suppuration, theoretically to prevent upward extension of the process into the subdiaphragmatic region. If lymphatic extension is the mechanism at fault, this seems to be unnecessary, but in the light of our relatively low incidence of subphrenic complications and until this matter has become more clearly settled, we see no reason to discontinue the use of Fowler's position in these patients.

Other intra-abdominal conditions that have been stressed in the literature as leading to subphrenic abscess are diseases of the stomach and duodenum (ruptured peptic ulcer) and diseases of the liver and gall bladder (cholecystitis and cholelithiasis). These conditions are extremely rare in childhood, and none of our patients can be classified in this category. Two patients, however, suffered from abscesses of the liver that broke into the subphrenic space. One of these had ulcers of the rectum leading to a septic pyelophlebitis and multiple liver abscesses and thence to a left antero-inferior subphrenic abscess. The other patient's liver abscesses derived from a septic thrombosis of the umbilical vein, ultimately at the age of three weeks—leading to a right inferior abscess. Both these patients died.

In 4 of our patients the infection appears to have been seeded by the blood stream. One patient had recurrent hordeola and subsequently developed a large right anterior abscess from which a hemolytic *Staphylococcus aureus* was cultured.

Another large abscess followed one month after an attack of suppurative otitis media. Two more were preceded by severe upper respiratory infection. The exact site in which the infection lodges in these cases is not clear. It seems unlikely that the metastatic infection begins as a localized inflammation of the peritoneum bordering the subphrenic spaces. It is probable that the organisms gain a foothold in the liver, forming an abscess or abscesses that subsequently break through adjacent subdiaphragmatic spaces, thus subsequently more extensive process on.

trauma was the initiating factor. This six-year-old boy, was struck on the right side by an automobile. Shortly thereafter there was a profuse amount of intra-abdominal hemorrhage associated with shock. This was treated conservatively with sedation in another

hospital. On the twelfth day the patient became febrile and complained of increasing right-sided pain and also pain in the right shoulder. Subsequently, we drained a right anterior abscess containing foul pus with a fecal odor from which a colon bacillus was cultured. It was thought that the original trauma was rupture of the liver with hematoma, but in the light of the subsequent bacteriology it is probable that some portion of the alimentary canal was also ruptured at the time of the accident, thus releasing the organisms that established the subsequent abscess.

ANATOMICAL LOCALIZATION

Since publication of the anatomical descriptions of Martinet⁶ and Barnard,⁷ it has become a common practice to define the subdiaphragmatic region as the space bordered above by the diaphragm and below by the transverse mesocolon. Thus, the abscesses occurring just below the liver, as well as those occurring between the liver and the diaphragm, are included within the boundaries of the subphrenic region.

The liver may be regarded as dividing this broader area into two regions, the suprahepatic and infrahepatic; each of these, in turn, is further divided by anatomic attachments into three spaces, making six in all. Beneath the diaphragm, the falciform ligament suspending the liver from that structure divides the suprahepatic area into essentially equal-sized right and left spaces. On the left, there is but a single superior space, but on the right the lateral reflexion of the coronary ligament divides the right space into a small posterior one and a large anterior one. Conversely, in the infrahepatic region, which is divided into right and left spaces by the round ligament and the ligament of the ductus venosus, there is but a single right inferior space, whereas on the left the gastrohepatic ligament divides the area into a posterior space, which is merely the upper portion of the lesser omental cavity, and a larger anterior space, between the liver and the stomach.

These divisions are present in infancy. No apparent anatomic variation from the adult is present in childhood to explain the relative rarity of infection of these spaces in children, with one possible exception. The suspensory ligaments of the liver are comparatively tighter and shorter in the young than in the old, thus tending to hold the liver more firmly upward against the diaphragm and squeezing closed the suprahepatic spaces.

Thus, there are six anatomically discrete intra-peritoneal subphrenic spaces in which abscess formation can occur. Clearly, anatomical knowledge of these areas will lead to more exact clinical localization of such infections, which in turn will

phragmatic retroperitoneal (extraserous) approach is clearly the procedure of choice.

In anterior-space infections, particularly in cases in which a mass is present, drainage can be effected extraserously by direct approach through the anterior abdominal wall. Incision may be either parallel to the costal margin or a short, vertical, high, paramedian one. The adhesions existing between the abscess and the anterior peritoneum allow drainage through them without soiling of the uninvolved general peritoneal cavity.

For the posterior-space infections, the so-called "retroperitoneal approach" was described by Ochsner and Graves¹¹ and has been utilized by Faxon¹². This involves resecting the twelfth rib and incising horizontally at the level of the spinous process of the first lumbar vertebra. The peritoneum is then dissected off the undersurface of the diaphragm until the cavity is reached.

In children, the exact anatomic localization, whether anterior or posterior, may be quite indefinite. Furthermore, this approach, although favorable for the superoposterior infections most frequently encountered in adults, is inadequate or at best unduly difficult if the infection lies in the anterior portion of the suprahepatic space, as is most frequently the case in children. We have therefore adopted and used with success a slightly different type of retroperitoneal approach. In this procedure, incision is made parallel to and just below the costal margin in the midaxillary line. The muscle layers are incised until the peritoneum is reached. Then, with blunt dissection, the peritoneum is peeled away from the undersurface of the diaphragm until the firm pyogenic wall is reached, when a finger is inserted in the abscess. Drainage tubes are inserted and the wound is closed with chromic-catgut sutures to the drain. This approach, although similar to that of Ochsner and Graves in that it is entirely extraserous, differs from it in that the incision is slightly lower and more lateral. The infection of both the anterior and posterior spaces can be readily drained, and the twelfth rib is spared.

In our series, 11 patients underwent operation for drainage of a subphrenic abscess, with 1 death—a mortality of 9 per cent. Of these patients, 5 had direct incisions into anterior-space infections, so that the abscess could be drained without opening the peritoneal cavity. The single death in this group occurred in a patient with phlebitis and multiple liver abscesses. Five other patients underwent a transthoracic approach. In 2, the pleural cavity was soiled, with resultant empyema; in 1, the peritoneum was opened, with exacerbation of the peritoneal infection; in 1, the abscess was

not found (perhaps fortunately) and was subsequently drained by the extraserous approach; whereas in only 1 was drainage satisfactorily accomplished without complications. Two patients were drained by the extraserous approach, one primarily and one secondarily after an unsuccessful transthoracic attempt. Both healed rapidly without complication.

To summarize, there were 5 cases that had a direct incision and 2 in which the peritoneum was stripped from the diaphragm, making 7 that for practical purposes had an extraserous approach. These patients had a much shorter and better convalescence than did those who had a trans-serous approach.

Thus, our experience with the transthoracic approach is entirely in line with that of Faxon and of Ochsner and his co-workers and has led us to abandon the procedure. Although there were no deaths in this series, the morbidity was high, and we must consider ourselves as enjoying better luck than management in this regard.

SUMMARY

A series of 14 children with subdiaphragmatic abscess is presented.

Although subphrenic abscess is not frequent in children, when present it represents a serious disease, with forbidding mortality if untreated.

Metastatic infection of the subphrenic spaces by way of the blood stream is commoner in children than in adults, and presents a characteristic symptom complex.

Exact preoperative localization of the abscess is more difficult in children than in adults, and anterior-space infections are commoner in adults.

The extraserous approach is by all odds the one of choice. Such a procedure with incision in the midaxillary line just below the costal margin is advocated for use in children.

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men, which may be localized on the side of the disease. Usually, some weight loss is present, and mild secondary anemia. Examination reveals a degree or two of fever, tachycardia, an elevation

approach the abscess. In the light of the overwhelming statistical evidence recently presented by Ochsner and DeBakey⁴ and Faxon,¹² it appears that there is no longer any justifiable reason for

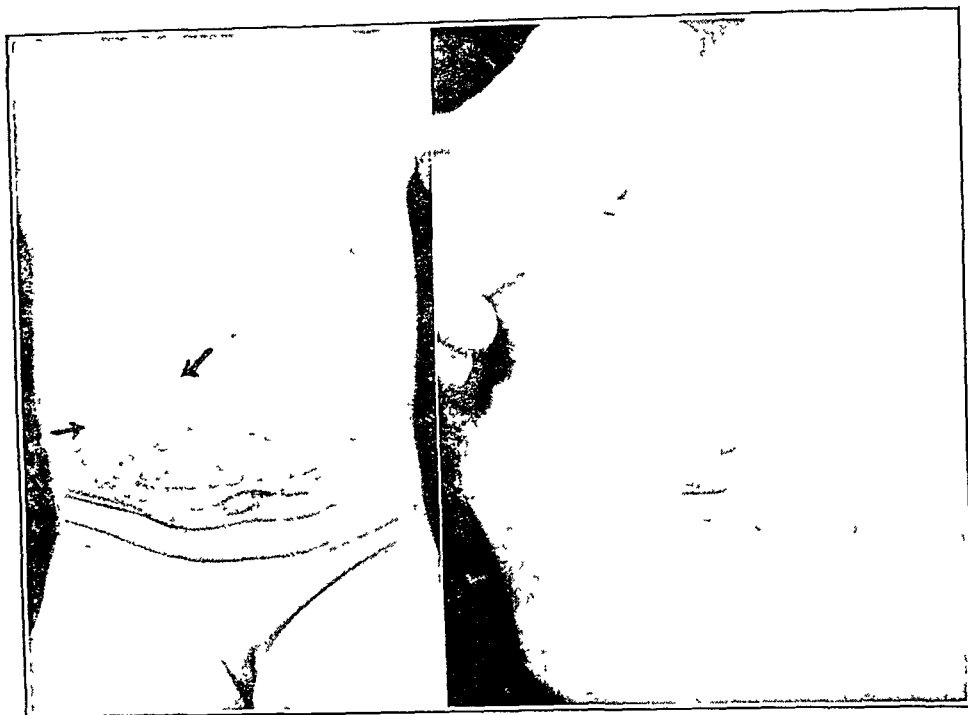


FIGURE 1.

Photographs of patient with large subdiaphragmatic abscess secondary to multiple hordeola, showing the right upper quadrant abdominal mass.

of the white-cell count and a diffuse, slightly tender mass in either the left or right upper quadrant, just under the costal margin.

The problem in diagnosis is that presented by an upper abdominal tumor. In 3 of our 4 patients the correct diagnosis was not made until the abscess was found at operation. It is our belief, however, that with such a history in a child with the constitutional signs of a chronic infectious disease and an upper abdominal mass, an accurate preoperative diagnosis can and should be made. Roentgenologic examination may be of corroborative value as in the postappendiceal variety.

TREATMENT

That early and adequate drainage is the correct treatment for subphrenic abscess is generally agreed. Until recent years, however, the best method of approaching these abscesses has been much debated. Three general types of operation have been evolved to solve the difficulties presented by an abscess in as relatively an inaccessible location as is the subphrenic space. These can be classified as transperitoneal, transpleural and extraserosus, according to the route used to

using any approach other than the extraserosus. The prolongation of the course, the marked increase in the incidence of complications and, above all, the much higher mortality rate associated with both the trans-serous approaches have been amply demonstrated. Thus, Faxon has shown that contamination of an uninvolved serous cavity during operative drainage increases the mortality to a level two and a half times as high as that in cases in which such contamination is avoided. In his series, contamination of a serous cavity carried a mortality of 62 per cent, whereas if neither cavity was contaminated, the mortality was 24 per cent. In the personal cases of Ochsner and DeBakey,⁴ the mortality of trans-serous approach was around 45 per cent, and that of the extraserosus approach was in the neighborhood of 10 per cent. The mortality in their large series of collected cases showed similar differences. Surgical rationale and statistical evidence alike demand that only an extraserosus route be employed in the drainage of these abscesses. That single or two-stage transthoracic procedures aiming to obliterate the pleural space are deceptively dangerous and fail to protect the pleural cavity is also clearly shown in these statistics. An infradia-

phragmatic retroperitoneal (extraserous) approach is clearly the procedure of choice.

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TIDAL DRAINAGE AND CYSTOMETRY IN THE TREATMENT OF SEPSIS ASSOCIATED WITH SPINAL-CORD INJURIES*

A Study of One Hundred and Sixty-Five Cases

DONALD MUNRO, M.D.†

BOSTON

SEPSIS is one of the most prolific causes of death and unnecessary disability in patients with spinal-cord injuries. Except for an occasional post-operative wound infection, it always originates as the result of inadequate care either of the urinary bladder or of the skin of the back or both. This paper deals with the genitourinary aspect of the problem, and presents my experiences with 165 patients with all levels and types of spinal-cord injury.

An understanding of the changes that take place in the human urinary bladder following a spinal-cord injury is impossible without an equal grasp of the physiology of urination. The classic work of Denny-Brown and Robertson¹ has been confirmed by myself,^{2,3} McLellan⁴ and many others, although some writers, like Langworthy and others^{5,6} do not agree with us in all details. All do agree, however, that the bladder is an organ the fundamental control of which is vested in two reflex arcs whose central connections are located in the sacral segments of the spinal cord. The peripheral part of the first is formed by the parasympathetic nerves in the pelvic plexus, and that of the second by the internal pudic nerve, which is a branch of the sacral plexus. The latter is a somatic nerve, and as such the impulses it carries are subject to voluntary control. There is also a third reflex arc, which comes into play only when the bladder is either anatomically or physiologically denervated. It lies completely within the confines of the bladder wall, is analogous to Auerbach's plexus, and is extremely inefficient. The motor impulses passing over the first two of these reflex arcs are subject to modification by other impulses reaching them by way of the long tracts in the cord and arising in the suprasegmental levels. In addition, the musculature of the bladder wall has a specialized attribute that is known as the stretch reflex. This is a mechanism whereby the individual muscle fibers, in response to the stimulus of having previously been stretched to their limit, retain the choice either of contracting sharply and emptying the bladder—a so-called "emptying contraction"—or of lengthening themselves and thereby in-

creasing the capacity of the reservoir. This stretch reflex allows a hollow organ such as the bladder, intestine or uterus to choose, as it were, between either one of two responses to a single stimulus. It is constantly being invoked in the normal bladder, and the addition of even small quantities of urine to whatever may be already present, regardless of amount, sets up a constant succession of stretch reflexes. Under appropriate circumstances and surroundings, these either turn into emptying contractions or, if the set-up is not suitable for urination, cause distention of the bladder without contraction of its wall and with an increase in its capacity. The impulses that reach the bladder from the brain are entirely inhibitory. They develop because of the dictates of civilization, one's early training, peculiar surroundings and the like, and serve to prevent any given stretch reflex from becoming an emptying contraction in circumstances that are not suitable. As is well known, they may inhibit emptying contractions so successfully as to lead to overstretching and pain and to make catheterization necessary. They are entirely outside of the conscious sphere and may exert a tremendous indirect influence on the life and activity of the individual, but act only to *stop* urination. On the other hand, facilitation of urination is entirely outside of the individual's power. It depends on and occurs only in the presence of an emptying contraction, is totally *segmental* in so far as anatomic connections go, and occurs only because the subject may fail to inhibit an emptying contraction and thus passively permit urination.

Although still disputed, the best evidence at this time seems to be that in man the sympathetic system, so far as the bladder is concerned, has to do *only* with transmission of pain. A series of personal observations made on 12 otherwise normal women who had had complete presacral neurectomies for dysmenorrhea has satisfied me that this statement is true. Cystometric observations made on their bladders before and after the neurectomies showed no change whatsoever in bladder function. It must therefore be concluded that the sympathetic system plays no part in the control of bladder activity. Others have made similar observations, and there can be little doubt that the earlier and more convenient theory of reciprocal para-

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sympathetic-sympathetic control of the bladder must be abandoned.

My first 36 cases of injury to all levels of cord and cauda equina came under my care before Denny-Brown and Robertson¹ had demonstrated in more detail the physiology that I have briefly sketched above. Twenty-six, or 72 per cent, developed major infections of the genitourinary tract. This was despite the use of all the then recognized methods of treating the bladder in these cases. To meet this difficulty the tidal-drainage apparatus was developed in 1935, and to ensure its success a separate cystometer was also constructed.² The former remained unchanged until it was modified by MacNeill and Bowler³ in 1940. By introducing the irrigating fluid directly into the bladder by way of a two-way catheter or a Y tube attached to the outer end of the single catheter while the other arm carried the outflow to the siphon curve and air seal, they enabled efficient irrigation of the bladder to be carried out with each cycle. This method allowed us to demonstrate that irrigation with a weak acid solution was much more effective in controlling bacteriuria than was alkaline potassium permanganate. I accordingly modified our apparatus to conform to MacNeill and Bowler's change and substituted 0.5 per cent acetic acid for 1:30,000 potassium permanganate as the irrigating fluid. This was a distinct step in advance, but the size and lack of transportability of the apparatus were still inconvenient. Furthermore, all attempts to combine the cystometer and tidal drainage into one apparatus failed. Thus, the making of the cystometrograms that were so essential to the successful working of the tidal drainage was neglected because of the trouble involved in sterilizing and setting up two separate pieces of apparatus. With the advent of Canada into the war and the need for transporting Canadian soldiers with spinal-cord injuries from England back to this continent, the problem of the continued use of the tidal-drainage apparatus during the transatlantic crossing was solved first by Stewart⁴ and later by Cone and Bridgers.⁵ They did their work in both England and Canada and have devised two further modifications of my apparatus, each of which is portable and also acts as a combined tidal-drainage apparatus and cystometer.

For the air seal Stewart substituted a capillary tube (Fig. 1), connecting this to the bladder outlet by way of a Carrel-Dakin glass connector with three side openings and one end opening. A manometer tube marked with graduations in any suitable way is attached to one side opening, the capillary tube to the second, and the end of the siphon tube to the third. The manometer tubing

is kept closed by a clamp on the rubber connection when the apparatus is used for tidal drainage, and is opened and used as a cystometer when cystometrograms are to be made. I have retained

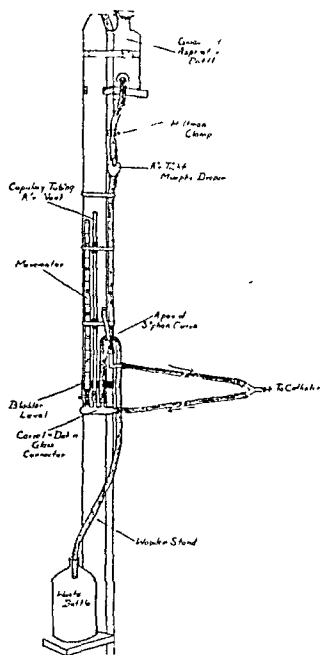


FIGURE 1. Munro's Tidal-Drainage Apparatus, as Modified by MacNeill and Bowler and by Stewart.

MacNeill and Bowler's modification with this apparatus, although neither Stewart in his model nor Cone and Bridgers in theirs did so originally. Both their apparatus work despite the fact that, during siphonage, air bubbles in through the capillary tube. The bubbles are so small, however, that they do not break the siphon until the bladder is empty. We have found, and Cone and Bridgers have warned, that care must be taken to see that the column of fluid in the descending arm of the siphon is of sufficient length to make enough negative pressure to empty the bladder. For various reasons, chiefly connected with ease of cleaning and comprehension on the part of nurses and house officers, I prefer and now use in all cases the apparatus as modified by MacNeill and Bowler and by Stewart. The materials required to make it are a 1000-cc. irrigator bottle with a bottom opening, an airtight Murphy dropper, two compression clamps, a glass Y tube, a piece of

glass tubing 70 cm. long with an inside diameter of not less than 3 mm., a capillary glass tube 70 cm. in length, a Carrel-Dakin glass connector

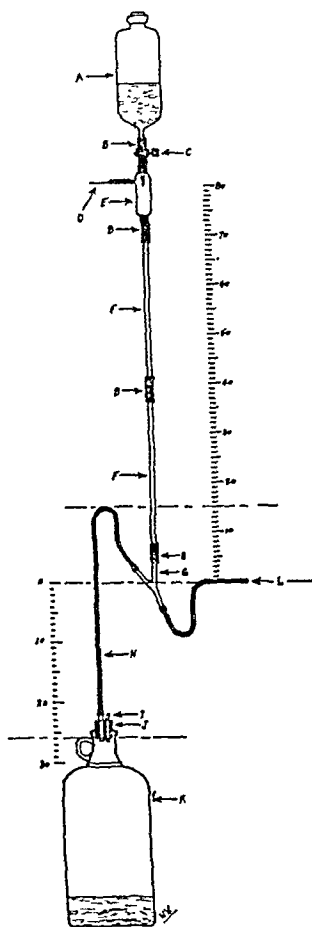


FIGURE 2. Munro's Tidal-Drainage Apparatus, as Modified by Cone and Bridgers.⁹ (Reproduced by permission of Surgery, Gynecology and Obstetrics.)

with three side openings and one end opening, a waste bottle, appropriate lengths of stethoscopic and acid-proof rubber tubing, glass connecting tubes and some form of board stand on which to clamp the apparatus and thus attach it to the bed. Cone and Bridgers's⁹ latest, and they assure me final, model (Fig. 2) is even more portable, has fewer parts, and is as efficient as Stewart's model. It is equally suitable for military use.

The built-in cystometer is fundamentally the same as the original U-tube apparatus (Fig. 3). All the cystometric observations made with it were carried out with the rate of fill set at 120 drops per minute or less. It is my conviction that similar observations are valueless unless they are made with an apparatus that approximates the normal physiologic rate of fill of the bladder. For this reason, observations made with a Rose cystometer or with others of the type in which the increments of bladder fill are set at 25, 50 or 100 cc.

at a time are probably not reliable. They cannot approximate in any way the conditions that exist when the bladder is being filled by the kidneys, and therefore conclusions based on such observations will of necessity be wrong. Neither should any dependence be placed on having the patient note when he first has a desire to void, nor is any information to be gained from it. In the first place, a conscious desire to void, if the patient is out of babyhood, will depend on his surroundings and a psychologic adjustment to them that

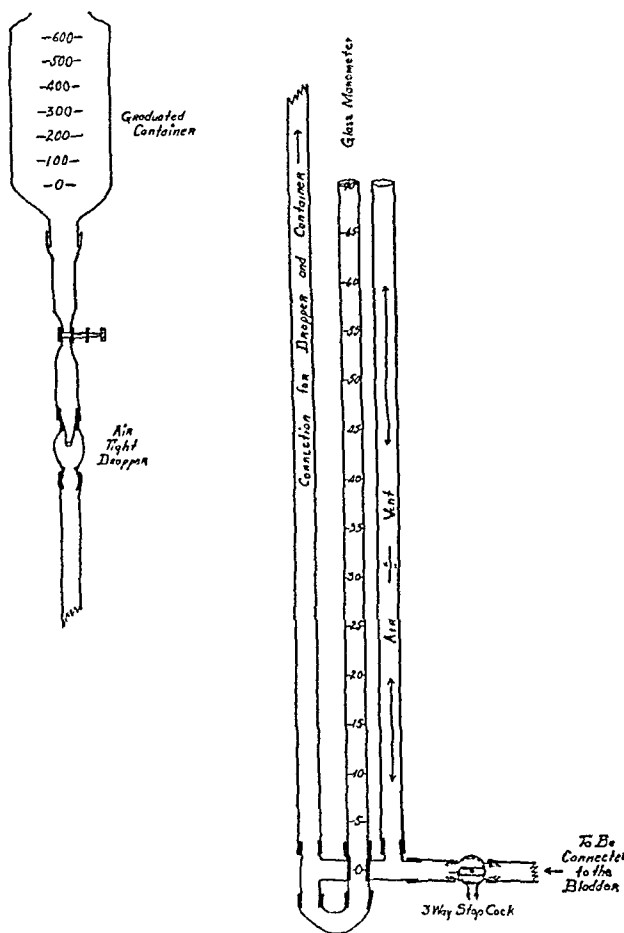


FIGURE 3. The Munro Cystometer.

differs in every patient and from time to time in the same patient. Not to recognize this is to fail to realize that civilization has set up certain standards of personal hygiene that at least in Anglo-Saxon countries are still in force. Conclusions drawn from information concerning when the patient has his first desire to void point not to the degree and kind of bladder function that he has, but rather to his ability to adjust himself to urinating in unusual circumstances.

The figures that follow are the results of studies made with the help of these various types of apparatus on 165 patients with injuries of the spinal cord and cauda equina. They include ex-

amples of edema, hematomyelia, contusion and partial or complete transection of all levels of the cord; stab wounds and bullet wounds of the cord and concussion from bullet wounds of the bony canal without direct cord involvement; compression by dislocated vertebrae, misplaced bone fragments and extra or subdural clots; and all ages of

Tidal Drainage Necessary But Not Used

Tidal drainage was needed but not used in 37 patients, including the 36 patients mentioned above as having been cared for before the apparatus had been invented (Table 1). Twenty-three had cervical injuries, 11 dorsolumbar, and 3 cauda equinal. Twenty-six patients died, all but 1 in the

TABLE 1 *Data on Cases in Which Tidal Drainage Was Needed but Not Used*

Type of Injury	48 Hr. Deaths	Genitourinary Tract Sepsis		Bedsore		No Sepsis	Total No of Cases
		Healed in Bed	Present at Discharge	Healed in Ward	Present at Discharge		
Cervical							
Living			1		1	4	5
Dead			7	—	2	7	18
Totals	9		8	0	3	11	23
Dorsolumbar							
Living	1	—	—	—	1	2	3
Dead	—	—	—	—	3	—	3
Totals	1	0	7	0	4	2	11
Cauda equinal							
Living	—	—	1	—	—	2	3
Dead	—	—	—	—	—	—	—
Totals	0	0	1	0	0	2	3
Grand totals	10	0	11	0	7	15	37

adhesive constriction of the cauda equina by organized blood clots. One hundred injuries were in the cervical region; 41 involved the dorsolumbar and sacral cord, and 24 the cauda equina. The mortality of the group as a whole was 43 per cent and varied from a high point of 56 per cent in the dorsolumbar group through 46 per cent in the cervical to a low point of 8 per cent in the cauda equinal patients. The fact that the highest death rate was associated with the dorsolumbar cord injuries and not, as might be expected, with the cervical ones should not be overlooked.

METHOD OF TREATMENT

Tidal Drainage Unnecessary

Twenty-seven patients had normal function of their genitourinary apparatus by the time they arrived in the hospital, despite the fact that they presented unmistakable clinical evidence of damage to the spinal cord or cauda equina. Seventeen had cervical injuries; 1 was dorsolumbar, and 9 cauda equinal. Among them were 1 case with a fractured atlas, 2 with stab wounds, 2 with radiculitis in addition to cord injury and 1 each with an arachnoidal hemorrhage and chronic arachnoiditis. There were no deaths and no complications except for a bed sore that developed in a syphilitic patient. This healed promptly on anti-syphilitic therapy.

hospital. Ten of these died within forty-eight hours of the receipt of the injury and consequently did not live long enough to develop sepsis. Seven died without evidence of genitourinary or other major sepsis. In 9 others, sepsis was present and unhealed at the time of death, an incidence of 56 per cent among those who survived the first forty-eight hours. Eleven patients were discharged alive. These included 3 with cervical, 7 with dorsolumbar and 1 with a cauda equinal injury. Three patients had major sepsis during their hospital stay. In one the sepsis was in the genitourinary tract only and in another this was combined with a septic bed sore; in the third case the source of sepsis was a bed sore alone. There were 8 patients who had no sepsis—4 with cervical and 2 each with dorsolumbar and cauda-equinal injuries. This is an incidence of sepsis among the living of 27 per cent.

When these figures are combined, it appears that 12 (44 per cent) of 27 patients who lived long enough to need but did not have treatment by tidal drainage had major sepsis at the time of death or discharge. This sepsis either involved the genitourinary tract or had its source in a bed sore or both. This incidence compares with the 72 per cent of similar major infections that developed in 36 patients during the course of their

stay. Both figures indicate the tremendous part played by the untreated genitourinary tract in causing death and disability in spinal-cord lesions

bedsores that had not healed by the time they died. One of these was directly traceable to neglect on the ward. The other five were present in spite of

TABLE 2. *Data on Cases in Which Tidal Drainage Was Needed and Used.*

TYPE OF INJURY	48 Hr DEATHS	GENITOURINARY-TRACT SEPSIS		BEDSORES		UNCONNECTED SEPSIS	NO SEPSIS	TOTAL NO. OF CASES
		HEALED ON WARD	PRESENT AT DISCHARGE	HEALED ON WARD	PRESENT AT DISCHARGE			
Cervical								
Living	-	4	2	-	-	2	24	32
Dead	12	1	-	-	1	2	12	28
Totals	12	5	2	0	1	4	36	60
Dorsolumbar								
Living	-	1	-	1	1	2	9	14
Dead	-	-	1	-	4	6	5	15
Totals	0	1	0	1	5	8	14	29
Cauda equinal								
Living	-	3	-	-	1	-	6	10
Dead	-	-	-	-	1	1	-	2
Totals	0	3	0	0	2	1	6	12
Grand totals	12	9	2	1	8	13	56	101

under what would otherwise be favorable circumstances.

Tidal Drainage Necessary and Used

Tidal drainage was necessary and used in 101 patients. Sixty had cervical, 29 dorsolumbar and 12 cauda-equinal injuries (Table 2). Forty-five patients died—all in the hospital. Of these, 12 died within forty-eight hours of the infliction of the injury and before they had time to develop any major sepsis.

Thirty-three patients developed major sepsis during their stay on the ward. Sixteen were discharged dead—a mortality of 50 per cent. In 9 of these patients neither the death nor the sepsis had any connection with the use of the tidal-drainage apparatus. This group was made up of 3 cases of ruptured urethra from instrumental perforation, 1 of ruptured bladder produced in the course of a lithopaxy, 1 of bed sore that developed at the site of a bruise sustained at the time of the injury and 4 of extensive bedsores that were already present at the time the patient came under my care. One of the last occurred in a patient who subsequently died of a ruptured urethra. In addition, 1 patient died as the result of a peritonitis caused by the rupture of an enterostomy fistula that had been made in order to treat the hypoproteinemia associated with a bad bed sore. The latter was healed at the time of the patient's death. One other patient died from femoral phlebitis and sagittal sinus thrombosis after he had recovered from a nonspecific urethritis. Six patients had

tidal drainage. Thus, out of 16 patients discharged dead, 5 (31 per cent) had sepsis in spite of the use of tidal drainage. Attention should, however, be called to the fact that in none of these cases did the sepsis involve the genitourinary tract.

Fifteen patients who developed major sepsis and were treated with tidal drainage survived (Table 3). In 3 the sepsis was present at admission, two patients having septic bedsores and the other having pyelitis and a renal stone. Both bedsores were healed, as was the pyelitis, and the kidney stone was removed by the time these patients left my care to resume earning a living. None of this would have been possible without tidal drainage. There were 10 cases of preventable genitourinary-tract sepsis and 2 of preventable bedsores in this group. All were healed at discharge. The genitourinary cases would not now occur and are traceable to inexperience with the apparatus. The other 2 patients represent failures. In one case there was a persistent bacteriuria, and in the other a failure to attain the proper functional end result in the bladder at the time of their discharge.¹ The first patient has been lost sight of. The other was senile at discharge and is now in a public institution. It can be concluded, therefore, that only 13 per cent of patients with nonfatal spinal-cord injuries who develop major sepsis will not have recovered from it at the time of their discharge if they are treated with tidal drainage during their hospital stay. Even this figure is unquestionably too pessimistic in the light of recent experience, and I venture to predict that within

a short time it will be possible to eliminate all major sepsis in such patients

If the above figures are combined and all possible cases included, it is apparent that of the 33 patients who developed major sepsis during their

by this and other means. It therefore seems reasonable to assume that this 13 per cent incidence can be reduced still further in the future, possibly even to the point of elimination of all such sepsis in spinal cord injuries that are properly handled

TABLE 3 Data on Cases of Major Sepsis in Which Tidal Drainage Was Needed and Used

TYPE OF INFECTION	SEPSIS NOT CAUSED BY TIDAL DRAINAGE				SEPSIS POSSIBLY CAUSED BY TIDAL DRAINAGE						TOTAL NO OF CASES		
	SEPSIS NOT CAUSED BY TIDAL DRAINAGE		SEPSIS CAUSED BY TIDAL DRAINAGE		PREVENTABLE SEPSIS	SEPSIS NOT HEALED AT DISCHARGE		SEPSIS HEALED AT DISCHARGE					
	LIVING	DEAD	LIVING	DEAD		LIVING	DEAD	LIVING	DEAD	LIVING	DEAD		
Genitourinary tract													
Urethritis	-	-	-	-	3	-	-	-	-	1	3	1	4
Epididymitis	-	-	-	-	5	-	-	-	-	1	5	1	6
Prostatitis	-	-	-	-	1	-	-	-	-	-	1	0	1
Pyelitis with or without kidney stone	-	-	1	-	1	-	-	-	-	-	2	0	2
Periurethral abscess	-	-	-	-	-	3	-	-	-	-	0	3	3
Ruptured bladder	-	-	-	-	-	1	-	-	-	-	0	1	1
Hemorrhagic nephritis	-	-	-	-	-	-	1	-	-	-	0	1	1
Persistent bacteriuria	-	-	-	-	-	-	1	-	-	-	1	0	1
Functional genitourinary failure	-	-	-	-	-	-	-	-	-	-	1	0	1
Bedsore													
Concomitant	-	-	-	5	-	-	-	-	-	-	0	5	5
Independent	-	2	2	-	2	-	3	-	1	-	4	6	10
Peritonitis	-	1	-	-	-	-	-	-	-	-	0	1	1
Totals	0	3	3	5	12	4	2	4	0	3	17*	12†	36‡

*Includes 2 duplicates

†Includes 1 duplicate

‡Includes 3 duplicates

stay on the ward, in 13 the sepsis was totally unconnected with the use of the tidal drainage apparatus. Nine of these patients died. Twelve other patients had genitourinary sepsis that was preventable. Thus, in only 8 patients out of the 33 that developed sepsis can the tidal drainage be considered a possible causative agent. This is a maximum occurrence rate of 24 per cent.

When the entire group of 101 patients is considered, the efficiency of tidal drainage becomes more apparent. After the elimination of the 12 patients who died within forty-eight hours of the receipt of their injury and of the 13 in whom the sepsis was completely unconnected with the use of the tidal drainage, there are 76 patients left, all of whom were treated with tidal drainage and 10 of whom had either genitourinary or bedsores sepsis at discharge. This, as previously stated, is an incidence of 13 per cent. Of these 10, only 6 died—a mortality from such sepsis of 8 per cent. These figures are comparable with the 40 per cent incidence of sepsis among the similar group of patients who were not treated with tidal drainage. As experience has been accumulating, it has been possible to eliminate urethritis, epididymitis and prostatitis, none of these conditions having developed in the last five years. Bedsores, too, have been practically eliminated in the last three years

from the start. The reduction in genitourinary sepsis already accomplished has not only made it possible to eliminate bedsores but has opened up new therapeutic approaches in dealing with the neural deficits of spinal cord injuries. This has led to a great diminution in permanent invalidism and an increase in the earning power on the part of these patients. The intelligent use of tidal drainage is now imperative in every patient who has sustained an injury to the spinal cord. There is no substitute for it.

COMPLICATIONS

I know of no contraindications to the use of tidal drainage. It will not run itself, however, and to work satisfactorily it must be set up properly and be adjusted correctly to the kind of bladder it is serving at the moment. Experience has demonstrated that cystometrograms must be made at least once a week on all patients with spinal cord injuries if they are to receive the utmost benefit from the apparatus. Common conditions that lead to other difficulties are looping of the rubber tubing in such a way as to form traps, air leaks within the apparatus, too short a descending arm of the siphon, failure to take down, clean, sterilize, and reassemble the apparatus once a week, failure to keep the irrigating solution sterile,

allowing the free end of the siphon tube to get below the top of the fluid in the waste bottle, improper instrumentation because of the absence of any complaint of pain on the part of the patient, the use of too large catheters and the presence of an active mass reflex.

Improper instrumentation, the use of too large catheters and the effect of an active mass reflex merit further comment. Instrumentation of an anesthetic urethra and bladder, particularly in the male patient, is, as the figures just quoted show, fraught with grave danger. The possibility of catheterizing a small or strictured urethra or of performing a lithopaxy without causing pain is one that is apt not to occur to the average physician or surgeon. As a result, he fails to realize until after the damage is done that the stylet catheter has not entered the bladder after a slight resistance, as he supposed, but that it has actually perforated the urethra. For the same reason, a fold of bladder wall caught and crushed in a lithorrite causes no pain but results in a perforated bladder and peritonitis.

All my cases of urethritis and epididymitis developed in the patients seen before I had appreciated the futility of and danger in trying to prevent leakage from the bladder by increasing the size of the catheter. A catheter that is too small works better than one that is too large. In the absence of any emptying contraction, leakage is controlled by the pressure of the internal sphincter on the catheter. This is as effective with a small as with a large catheter. Furthermore, the small one has the additional advantage of permitting urethral drainage and thus preventing backing up into and infection of the urethral glands and epididymis. Concerning the type of catheter, my preference is for a rubber rectal tube of proper size in the male and a mushroom-tipped rubber catheter in the female. The location of the hole in the end of the rectal tube instead of the side of the catheter is a great advantage. I have frequently used, however, and many surgeons prefer, either one-way or two-way Foley catheters, but if such a catheter is used in long-standing cases, great care must be taken to see that the expansile bulb that holds it in place is pushed inward and kept from touching the mucous membrane of the bladder. If this is not done, a pressure sore will develop in the bladder wall at the point of contact.

Inasmuch as the reflex bladder can be stimulated to empty itself by pressure or massage through the abdominal wall whenever there is any urine in it, an active mass reflex can and frequently does cause an emptying contraction to develop at highly unexpected and troublesome

moments. In such a reflex, the motor response—set up by a minimal sensory stimulus anywhere on the lower extremities—spreads to involve the muscles of the legs and the abdominal wall. It is this contraction of the abdominal muscles that stimulates the bladder and causes it to empty. Tidal drainage is as yet inefficient in caring for such a condition, and I am not certain how best to deal with this problem. However, some success has been attained by approaching it from the point of view of controlling the reflex rather than draining the bladder, but it has not been possible to reach any final conclusions as yet.

URINE CULTURES

Every one of my patients has had a urine culture once a week during the time he remained on tidal drainage. In addition to a tremendous variety of other organisms, either colon or proteus bacilli have always been grown from these urines so long as the catheter remained in place. Cultures are made by an as yet unpublished method devised by Dr. Daniel W. Badal, a former assistant of mine. This method reduces contaminants to a minimum. In this way it has been learned that, under ordinary circumstances and regardless of whether or not the bladder is normal, the urine of patients with inlying catheters remains sterile for the first seventy-two hours. After that time bacteriuria develops in *every* case. With the proper use of tidal drainage in the abnormal bladder, however, this bacteriuria remains a bacteriuria and does not produce significant cystitis, ureteritis or pyelitis. This has held true even in the cases in which death followed the prolonged use of tidal drainage. Figure 4 shows the normal gross appearance of the genitourinary tract in 2 cases in each of which death occurred after one and a half years of tidal drainage, one of sepsis from a bed sore and the other of acute peritonitis. This is characteristic of all similar cases.

I have used all recommended methods and medicines in an endeavor to sterilize the urines of patients with spinal-cord injuries while on tidal drainage. Mandelic acid, the arsphenamines intravenously and all the sulfonamides, both by mouth and in solution as an irrigating fluid, as well as innumerable other solutions including aqueous iodine, have all failed as long as the indwelling catheter remained in place or as long as a renal or bladder stone was present. With their removal, and provided the patient survived, the urine sterilized itself without medication in every case except one. In that case, the patient was clinically well but still had a bacteriuria at discharge. The end result is not known in this case because follow-up studies could not be made. I have now aban-

done as useless all forms of medication designed to sterilize the urine of patients who are being treated with tidal drainage except for the medicinal effect produced by forcing fluids by mouth at the rate of 5000 cc. every twenty-four hours for

work that is not as yet finished even suggests that with proper training and the use of a rubber urinal the patient may be able to dispense permanently with the indwelling catheter. In the former case, however, he must learn to take down,

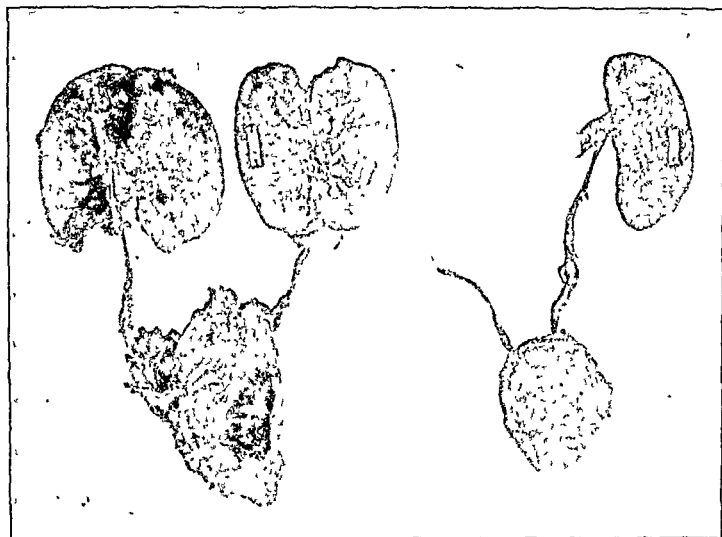


FIGURE 4. *Effect of Prolonged Tidal Drainage.*
The gross appearance of kidneys from two patients, each of whom had been treated with tidal drainage for one and a half years.

adults, and by the use of either 1:30,000 potassium permanganate or 0.5 per cent acetic acid as an irrigating solution—preferably the latter. In the absence of residual urine, this bacteriuria is of no clinical significance. With removal of the indwelling catheter, it clears up without further aid.

EXPECTED GENITOURINARY END RESULTS

Patients who have any variety of injury to the spinal cord or cauda equina that is not fatal within the first week now have the right to demand certain genitourinary end results. If there is destruction of the sacral segments or roots, the bladder is useless and it may be necessary to consider eventual transplantation of the ureters to the outside and the permanent use of urinals. If the patient has a transected cord and the mass reflex is not too active, he should expect to be able to lead an active and practically unrestricted wheel-chair life or its equivalent. Moreover, he should certainly expect to be free of the tidal-drainage apparatus except at night. Some recent

clean, sterilize, and set up the apparatus, as well as to fix an indwelling catheter in place in a sterile manner. He will have a bacteriuria, but should not have either clinical cystitis or pyelitis. If the mass reflex is active, tidal drainage will not function sufficiently well to permit such a patient to live outside of an institution at present. All other patients with nonfatal spinal-cord injuries should expect to have a completely normal genitourinary tract with sterile urine at the time of their discharge from institutional care. In addition, the development of bedsores during the patient's recumbency and regardless of the type or level of his cord injury should be cut to the vanishing point by the proper use of tidal drainage and other means, and death from genitourinary sepsis following spinal-cord injury should be eliminated.

SUMMARY

Tidal drainage was not needed in 27 of 165 patients with all types and levels of spinal cord injury.

Tidal drainage was needed but was not used in 37 of these 165 patients. Ten died within forty-eight hours of the receipt of the injury. Twelve out of the remaining 27 had major sepsis at the time of their death or discharge—an incidence of 44 per cent.

Tidal drainage was needed and used in 101 patients. Twelve died within forty-eight hours of the receipt of the injury. Thirty-three of the remaining 89 had major sepsis during their stay on the ward. In 13 the genitourinary sepsis was preventable and in 13 the sepsis had no connection with the use of the tidal drainage. Thus, 76 patients are left, all of whom were treated with tidal drainage, and 10 of whom had either genitourinary or bedsores sepsis at discharge—an incidence of 13 per cent.

A brief description of the newest tidal-drainage apparatus with a built-in cystometer is given.

Certain minimal genitourinary end results applicable to patients with injuries of the spinal cord or cauda equina are listed.

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CLINICAL NOTE

A HIP-NAIL DETERMINER

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THE instrument whose description follows allows automatic calculation of the length of the nail, pin or screw that should be inserted into

a simple mathematical slide rule transformed for the purpose of giving, by two measurements on the x-ray film and one movement of the slide, a direct calculation of the proper length of nail, pin or screw to be used. The particular instrument that we have been successfully using for over two years is shown in Figure 1. The directions for its use are as follows:

- (1) Set 0 on the B scale opposite 9.0 on the A scale (9.0 cm. is the actual length of the direction-finder).
- (2) Place the determiner against the x-ray film (Fig.

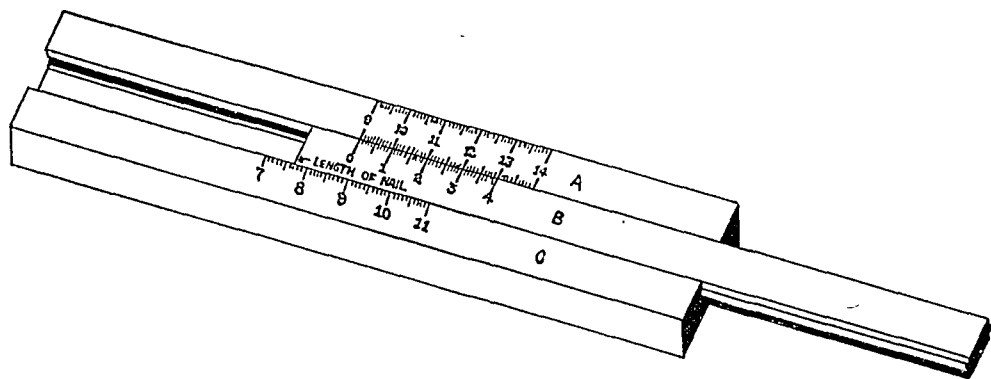


FIGURE 1.

the head of the femur to accomplish internal fixation of a fracture of the femoral neck. There are now in use many known techniques by which this internal fixation is performed, and, because in the one¹ which we chose to use a direction-finder is employed, we explored the possibility of applying

2), and read off the number on the B scale corresponding to the length of the direction-finder from the left-hand end of the determiner.

(3) Place the determiner against the x-ray film and measure the distance from the proximal end of the direction-finder to the end of the femoral head on the A scale.

(4) Move the slide so that the B-scale number determined in (2) is opposite the A-scale number determined in (3).

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(5) The point where the left hand end of the slide falls on the C scale determines the length of nail to be used.

The distance between the proximal end of the nail and the tip of the femoral head, which we have preferred to make 1.5 cm., may be as widely varied as desired in the construction of the de-

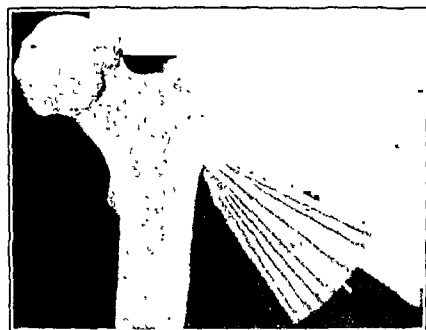


FIGURE 2. X-Ray Film with the Engel-May Direction Finder in Place.

terminer, depending on how much impaction one expects or prefers and on how nearly the head of the nail, pin or screw is made flush with the surface of the femur below the greater trochanter. Furthermore, although the length of the Engel-May direction-finder happens to be 9.0 cm., it should be pointed out that, according to the length of the particular direction-finder or radio-opaque stenciled metal plate² that one prefers to employ, a scale can be empirically devised to give the proper calculated results. The instrument can be readily fashioned as follows:

An ordinary wooden slide rule (price, 50 cents to \$1.00) is sanded well to receive the numbers. An A scale is

constructed in centimeters up to 14 or 15 cm.—in pencil for all preliminary work and in India ink for the final product (the first nine centimeters—the length of the Engel-May finder—are not marked, since there is always some magnification of the finder on the x-ray film). On the slide next to the A scale a distance of 1.5 cm. (the preferred distance from the tip of the pin to the tip of the femoral head when the head of the pin is flush with the bone) is measured from its tip, and starting there, a B scale is made in centimeters. After the A and B scales have been constructed, a C scale is made by setting 1.3 on the B scale opposite certain numbers on the A scale, as follows:

9.8 equals	7.5 - C
10.4 equals	8.0 - C
11.0 equals	8.5 - C
11.6 equals	9.0 - C
12.2 equals	9.5 - C
12.8 equals	10.0 - C
13.4 equals	10.5 - C

These points should be *marked and labeled*, and the intervening points interpolated. Obviously, the C scale is not a centimeter scale. For convenience in the operating room the five directions given above are printed on the reverse side of the slide rule, and the whole instrument is varnished, care being taken not to affect the slide.

In order to test the accuracy of this device one has only to set up practical problems, remembering that few femoral necks in practice are shorter than 8.8 or longer than 12.0 cm., and that fortunately, in most cases, the shorter the hip, the smaller the x-ray magnification, and the longer the hip, the greater the magnification. The margin of error in the practical application of this instrument, provided it is properly used, is well within the range of safety.

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MEDICAL PROGRESS

PERIPHERAL VASCULAR DISEASE*

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PERIPHERAL vascular disease is assuming greater importance in medicine, not only because it is becoming commoner in the ageing population,¹ but also because it is being more frequently recognized as a sign of possible remote or widespread disease. Recent articles have emphasized the fact that not only arteriosclerosis but also thromboangiitis obliterans, Raynaud's disease and scleroderma may be accompanied by vascular disturbances in the lungs,²⁻⁴ heart^{2, 5} or brain.^{2, 6, 7} Furthermore, it has been pointed out that systemic diseases such as periarteritis nodosa,⁸ Boeck's sarcoid,^{9, 10} lupus erythematosus and dermatomyositis¹¹ may manifest themselves by vascular signs and symptoms in the extremities. However, in spite of an enlarging interest in the subject, progress in the understanding of the fundamental nature of the various peripheral vascular diseases has been slow. For this reason preventive and therapeutic measures have been largely nonspecific and symptomatic. The first part of this review will attempt to summarize the current concepts of the etiology and pathology of diseases of the peripheral arteries, the second to analyze some recent suggestions for their symptomatic treatment, the third to give a brief résumé of peripheral vascular diseases resulting from exposure to cold, and the last to present the newer aspects of diseases of the veins, especially as they concern the practitioner of internal medicine.

DISEASES OF THE PERIPHERAL ARTERIES

Atherosclerosis, by all odds, is the most prevalent and economically the most important vascular disease of adults. Recent studies¹² indicate that this disease is the result of a selective invasion of the arterial intima by, and the localization therein of, cholesterol-laden (foam) cells derived from the reticuloendothelial system. Following the breakdown of these cells, de-esterified cholesterol is deposited in the subintima as plaques, which act as foreign bodies. Vascularization, fibrosis and

calcification of such plaques occur in varying degrees to produce the familiar lesions of atherosclerosis. Atheromatous plaques may slowly enlarge to compromise the lumens of the vessels and cause gradual occlusion, or may suddenly undergo subendothelial hemorrhage and cause rapid occlusion.¹³

Hereditary predisposition to atherosclerosis and to the diseases with which it is commonly associated must be of great significance in determining its occurrence. Also, the fact that various hypercholesteremic disorders, such as diabetes mellitus,^{14, 15} hypothyroidism,¹⁶ nephrosis¹⁷ and various xanthomas,¹⁸ are so frequently complicated by atherosclerosis indicates that a derangement of lipid metabolism plays a fundamental part in its etiology. Likewise, the greater frequency of atherosclerosis in arteries under increased intravascular tension, whether due merely to hydrostatic effects (in the lower half of the body¹⁹) or to systemic (essential²⁰) or pulmonary (mitral stenotic²¹ or emphysematous²²) hypertension, suggests the importance of high arterial pressure in the causation of the disease. The etiologic roles of compression and collapse of the vasa vasorum, and of depressed oxygen dissociation properties of the blood,²³ although of great interest, are less clear.

Thromboangiitis obliterans etiologically remains a mystery. Its pathology suggests that it is an infection involving the veins and arteries in a proliferative inflammatory reaction beginning in the intima, extending to the entire vessel wall and leading to occlusive thrombosis with subsequent fibrous organization.²⁴ Streptococci,²⁵ trichophytons^{26, 27} and *Rickettsia prowazekii*²⁸ all have been suggested as possible etiologic agents. Its predilection for males, young adults, Jews and tobacco-smokers is generally recognized but unexplained. Thrombophlebitis migrans is a frequent precursor or concomitant, but produces little local or systemic reaction, although pulmonary embolism from this source has been known to occur.²⁹

The course of thromboangiitis obliterans is extremely variable,²⁴ and its distribution patchy; it may be slowly or rapidly progressive depending on whether it involves small segments of a single vessel or large segments of a number of vessels. At

*The articles in the medical progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C. Thomas Company, 1942 \$5.00).

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present there is no indication that any single preventive or therapeutic measure is specific. Equally good therapeutic results are achieved by the simplest hygienic measures and the least meddlesome procedures.³⁰

Raynaud's disease classically appears in asthenic young women in whom attacks of acral vasospasm occur in response to chilling and to emotional stimuli. Accordingly, its manifestations are thought to be due to an abnormal vasoconstrictor response to local cold^{31,32} or to a hyper-reactivity of the sympathetic nervous system.³³ However, its frequent association with scleroderma,³⁴ calcification of subcutaneous tissues,^{4,35} decalcification of bone,⁴ pulmonary fibrosis^{3,4} and widespread vascular disease^{8,11} suggests that Raynaud's phenomenon, in many cases, is merely a local manifestation of a more serious systemic disorder.

Periarteritis (polyarteritis) nodosa continues to be reported in the literature with ever-increasing frequency.³⁶ Peripheral vascular involvement, when present, may be characterized by palpable nodules along the course of superficial arteries, pulsating subcutaneous nodules (aneurysms), obliteration of the pulse in small arteries and Raynaud's phenomenon.⁸ Its pathology is essentially a fibrinoid necrosis of the arterial wall with an associated acute, subacute or healing inflammatory cellular reaction that also involves the perivascular tissues.

It has been pointed out that the frequent association of periarteritis with asthma, urticaria and eosinophilia suggests a hypersensitive background in its causation.³⁷⁻³⁹ Lesions typical of periarteritis are said to have appeared in patients who had hyper-reactions after the administration of foreign serum, sulfonamide therapy or both.^{37,38} They have also been reproduced in the laboratory rabbit by injecting a single large dose of horse serum.³⁹ These observations arouse speculation whether the increasing incidence of periarteritis may be due to the increasing use of serums, vaccines and sulfonamide drugs.

SYMPTOMATIC TREATMENT OF OCCLUSIVE ARTERIAL DISEASE

The ischemia caused by arterial occlusion is probably the most potent stimulus for the promotion of collateral circulation,⁴⁰ which, in turn, is certainly the most important factor in determining the ultimate effects of an arterial occlusion.⁴¹ These facts are still little appreciated, if one is to judge from the great variety of therapeutic measures reported to be of more or less specific value in the treatment of occlusive arterial disease.

Intermittent venous occlusion is claimed to be beneficial,⁴² not only because it may be followed (after release) by reactive hyperemia,⁴³ but also because it has been reported to produce an increase in arterial blood flow during the period of obstruction.⁴⁴ It has recently been shown, both in man⁴⁵ and in animals,^{46,47} that venous obstruction decreases arterial blood flow during the period when venous pressure is increased (above about 30 mm. of mercury). It is true that following the release of venous obstruction there is a short period of reactive hyperemia in normal limbs, but compared with that following the release of arterial occlusion it is small in amount,⁴³ and probably does not repay the blood-flow debt incurred during the venous obstruction.⁴⁸ Furthermore, following prolonged periods of continuous^{43,45} or intermittent^{45,48} venous obstruction there is no lasting increase in resting blood flow.

In limbs with severe arterial impairment, the mechanism of reactive hyperemia is apparently being constantly invoked. This has been shown by the fact that after the circulation in such limbs has been completely occluded for periods up to fifteen minutes, there is no increase in blood flow (on release of the circulation) over the previous resting level.⁴⁹ This is in sharp contrast to the marked reactive hyperemia that occurs in normal limbs following the release of arterial occlusion.⁵⁰ It indicates that these diseased limbs have constantly as great a blood flow as is possible in response to the stimulus of blood-flow deprivation. It shows the futility of attempting to increase arterial blood flow in such limbs by reactive hyperemia, especially with such an ineffective method as venous occlusion. There is a possibility that distending the capillary bed may be beneficial in these cases, either directly, or indirectly, by favorably affecting lymph flow, but this has not yet been proved.

Recent studies indicate that positive external pressure greatly decreases blood flow, whereas negative external pressure does not significantly increase it in the limbs.⁵¹ For these reasons, it seems doubtful that *alternate suction-pressure techniques* are of benefit in improving blood flow.

Producing *reflex vasodilatation* by warming the body increases the blood flow in the forearm and calf as well as in the hands and feet.⁵² Provided diseased arteries are capable of further dilatation, warming the body should be helpful temporarily in improving the nourishment of the tissues. However, local heat, unless properly controlled, may increase the metabolic demands of the tissues out of proportion to the available blood supply,⁵³ and thereby do more harm than good. The danger

of burning limbs in which the circulation is minimal also needs constant emphasis.

The role of the sympathetic nervous system is much more important in determining the blood flow in the skin areas of the extremities than in the muscular areas.^{52, 54, 55} However, it appears that, in the forearm and calf, sympathetic nervous activity can alter the blood flow as much as 200 to 300 per cent.⁵² Apparently in these parts active vasodilatation, as well as vasoconstriction, is mediated over the sympathetic nervous system. These physiologic considerations should be borne in mind when surgical sympathectomy is contemplated for the relief of peripheral arterial disease.

Surgical sympathectomy is most clearly indicated when it can be shown that reflex sympathetic vasoconstriction plays an important role in causing ischemia.^{41, 56} This may be demonstrated by producing reflex vasodilatation (warming the body) or by functional sympathetic block (producing spinal anesthesia, or procainizing the sympathetic ganglions or peripheral nerves). If there is a definite improvement in blood flow after such a procedure, it is reasonable to expect a similar result after surgical sympathectomy. It has been suggested that sympathectomy may also promote the development of collateral circulation.⁵⁷

Following preganglionic sympathectomy the skin of extremities with arterial disease often improves, both in color and temperature. However, it has been questioned whether this necessarily indicates improvement in general nutrition in the limb.⁵⁸ Furthermore, as yet no convincing studies have appeared demonstrating that blood flow is improved in sympathectomized muscular areas as compared with unsympathectomized control areas (in the opposite limb when there is comparable arterial disease). Symptomatic improvement, and increased claudication times following surgical operation and bed rest, although suggestive,^{56, 57, 59} are not conclusive evidence of an improvement in circulation due to the operation.

The natural reparative processes of the body make it necessary to control rigidly the experimental trial of any therapeutic procedure for peripheral vascular disease. This is especially true when such a specific procedure is applied along with various nonspecific measures, such as bed rest, warmth and general hygiene. Finally, when the procedure in question operates generally in the body, making it impossible to compare its effects in one part with the status in a control part, the physician can have recourse only to the statistical method in a large series of patients alternately treated with the procedure. Until studies of this kind are done there will continue to be

disagreement as to the value of various *hormones, tissue extracts* and *intravenous solutions*.

PERIPHERAL VASCULAR DISEASES DUE TO EXPOSURE TO COLD

Submarine warfare has focused attention on *immersion foot*—a vascular disease of the extremities due to exposure. This condition, seen in survivors from ships torpedoed in the cold waters of the North Atlantic, is in no way different in its etiology and pathology from the trench foot observed in the last war.⁶⁰ In either case, the lesion is caused by temperatures sufficient to chill but not to freeze the tissues. Experimentally, exposing an extremity to cold causes formation of edema fluid with a relatively high protein concentration.⁶¹ This is interpreted as meaning that cold insufficient to freeze the tissues can produce an increase in capillary permeability and an inflammatory exudate. The edema formation is roughly proportional to the degree of cold and to the duration of exposure. Also, experimentally cooling the peripheral nerves may abolish sensory, motor, vasomotor and sudomotor functions.⁶²

Shipwrecked sailors exposed to cold for prolonged periods develop swollen, discolored, anesthetic and even pulseless extremities, the distal portions usually being affected most severely.^{60, 63-66} Dependency and immobility of the limbs add to the swelling, and possibly to the severity of the vascular lesions. Constricting footgear, under these conditions, also seems to increase the resultant damage. Men habitually exposed to warm environments, such as those of the Mediterranean and African races, and those employed in boiler rooms, apparently are more susceptible than others to immersion foot, but there is no evidence that this susceptibility is due to a pre-existing vascular abnormality.⁶⁰ However, one episode of immersion foot apparently renders the feet less resistant to further exposure to cold.⁶⁷

In the severest cases reported to date, the feet and lower legs have been swollen and anesthetic almost to the knees, and the distal halves of the feet have appeared gangrenous. A low-grade fever is not uncommon for the first few days after rescue and is no cause for alarm. A high temperature, usually indicative of infection, is more serious.

After rescue and warming of the body the limbs become hyperemic and remain so for several days to six weeks. The hyperemia is associated with an increase in edema formation and occasionally with the appearance of blebs containing serous or serosanguineous fluid. In cases in which the hyperemia is most intense, sweating and sensation are usually absent, and subcutaneous hem-

orrhages may occur. When the hyperemia fades, the skin of the feet desquamates. Gangrene, if present, is rarely more than superficial, but infection, either in the presence or absence of gangrene, constitutes a serious complication.

The anesthesia disappears quickly in the proximal areas but only slowly in the distal areas, where nerve damage is more severe. A burning, tingling pain accompanies the return of sensation and often persists until nerve regeneration is complete. Sweating and sensation reappear in the same areas practically simultaneously.

Treatment should be directed toward avoidance of further injury, reduction of the hyperemia and edema, and maintenance of strict asepsis. The patient should be lifted aboard the rescuing vessel and body warmth restored, but the limbs should be kept cool and elevated until the hyperemia subsides. Application of cold packs is the most effective means of cooling, but spraying water into the air current of a fan directed toward the feet or simply exposing the limbs to a room temperature of 70°F. may suffice. Moderate cooling reduces hyperemia, promotes resorption of edema fluid and blebs, prevents hemorrhage into the tissues and minimizes pain. If pain is not diminished or abolished by cooling, opiates are employed, and even nerve crush may be considered.⁶⁵

Sympathectomy is not advisable in the hyperemic stage because blood flow in the large vessels is already maximal. However, if after recovery there is evidence of organic or functional (vasoconstrictor) arterial disease, sympathectomy may be considered.⁶⁷

Survivors of ships torpedoed in subtropical or tropical waters also develop swollen, painful feet, but do not present the cutaneous vascular changes seen in immersion foot.⁶⁸ These men, subjected to intense heat and short water rations, become dehydrated and develop nutritional deficiency due to an inability to swallow the concentrated emergency rations. Cheilitis, glossitis and stomatitis, in addition to peripheral neuritis, suggest that vitamin B deficiency is an important factor. Thus protein and vitamin deficiencies probably contribute to the edema and the pain.

Chilblain and *pernio* (erythrocyanosis) deserve mention because of their relation to immersion foot.⁶⁷ Although also due to exposure to cold, they are seen, in contrast to immersion foot, most commonly in patients with a history of cool limbs in summer as well as winter. This suggests that they are liable to occur on the basis of a pre-existing circulatory disturbance in the limbs.

Chilblain⁶⁷ occurs on the dorsum of the fingers, hands or feet as a localized, warm, red, pruritic swelling that may disappear in a few days, but

more often becomes an indolent lesion, dull red or violaceous, proceeding to painful bleb formation or ulceration. It is due to repeated or prolonged exposure to cold insufficient to freeze the tissues and appears (in temperate zones) at the onset of cold weather, recurring each year in the same exposed areas of the body.

Pernio,^{67 69} an essentially similar lesion involving the lower parts of the legs, occurs especially in women because their mode of dress affords inadequate protection for their legs against cool weather.

Strictly speaking, *frostbite*, in contradistinction to immersion foot, chilblain and pernio, is due to freezing of the tissues, with mechanical disruption of cell structure.⁷⁰ Actually, however, it frequently occurs in association with one of the other syndromes. When the freezing is superficial, thawing is followed by the typical cutaneous response to injury, namely local reddening, wheal and flare, but, when the skin is frozen more extensively, or when the subcutaneous tissues are involved, it is accompanied by bleb formation, or by necrosis and ulceration. Thawing should be slow, not only to lessen the pain and edema formation, but also to reduce the secondary tissue damage that occurs during the excessive local reaction when thawing is too rapid. Thus the time honored remedy of applying cold (slight relative warmth) to a frozen area has a rational basis. Rubbing or friction, on the other hand, is not recommended, since it but further traumatizes already damaged tissues.

DISEASES OF THE PERIPHERAL VEINS

Varicose veins, still numerically the most important problem of the peripheral venous system, are best treated by surgical ligation, excision or injection.⁷¹ Unless, however, the possible variations in the superficial venous drainage of the limbs are taken into account at the time of operation, varicosities are liable to recur.^{71 72} Furthermore, following therapeutic injection of the superficial veins, chemical thrombosis may extend into the communicating and deep veins and cause post-treatment edema and pain. This complication has been treated by the use of the anticoagulant heparin.⁷³

Varicose veins, when extensive, may be responsible for cardiovascular symptoms such as fatigue, exertional dyspnea, dizziness, precordial distress and syncope in the orthostatic position.⁷¹ In this position the return of blood through superficial, as contrasted with deep, veins in the legs is relatively slight, and is but little affected by muscular activity, even in normal persons.⁷⁵ When there are varicose veins with incompetent or even throm-

bosed^{76, 77} valves, actual stagnation of blood occurs in the varices, which may pool a sizable portion of the total blood volume. This results in an insufficient return of venous blood to the heart and causes symptoms of orthostatic collapse. Some patients have been greatly relieved of these symptoms following proper treatment of their varicose veins.⁷⁴

Phlebothrombosis is an insidious disorder, since it is accompanied by little or no local inflammatory reaction to signal its presence or to fix the thrombus in situ.⁷⁷ Consequently, its first sign may be the occurrence of embolism in the lungs.⁷⁸⁻⁸⁰ Conditions predisposing to venous thrombosis, such as myocardial failure, malignancy, obesity, debility, severe infections, varicosities, trauma and surgery, probably operate in a variety of ways.^{77, 80, 81} One of these certainly is to slow markedly the circulation in the limbs.^{82, 83} Postoperatively, maximal slowing of the circulation in the legs is said to coincide with the time when phlebothrombosis and pulmonary embolism most commonly develop.⁸³ Other factors recently suggested as possibly important in predisposing to phlebothrombosis include the occurrence of hyperprothrombinemia after surgical operations⁸⁴ and the development of cold agglutinins after certain infections.⁸⁵

Deep breathing, bicycle exercises, and flexion and extension of the extremities are useful in speeding the circulation and lessening the danger of venous thrombosis.^{82, 86} Some authors⁸⁷ have recommended the administration of thyroid for this purpose. Unfortunately in debilitated and especially in cardiac patients, these procedures are difficult to carry out. However, measurement of the circumference of the limbs and the application of Homans's maneuver — dorsiflexion of the foot to elicit pain in the calf or popliteal space or both — can and should be done daily in order to detect the presence of phlebothrombosis.⁷⁹ Determinations of venous pressure, especially after exercise of the limb, may indicate the presence of local venous obstruction.⁸⁸ Venography has also been recommended to show the location and extent of the lesions,⁸⁹ but even if

venogram is negative, thrombosis is not.⁷⁹ It is also well to remember that angiography is not without danger of serious or even fatal reactions, and that rigid precautions must be observed in the use of contrast media in angiography. The diagnosis of diseases of the venous system by the treatment of the disease is longer and is of so much importance that the design of the separation

has formed, must take precedence over therapeutic procedures against phlebothrombosis per se. Therefore, active or passive motion is contraindicated when it seems probable that thrombosis has occurred.⁷⁷ Moreover, rest, immobility, local heat and elevation of the limbs may be inadequate in preventing embolization.⁹¹ For these reasons a more positive approach, venous ligation, is recommended. It has been emphasized that unilateral ligation may not be sufficient, since the predisposing factors to phlebothrombosis operate generally, and quite often thrombosis is present in both legs.⁷⁹ Furthermore, embolization is more liable to occur from the less obviously involved (less symptomatic) limb. Finally, ligation should be performed high enough to preclude the possibility of embolization from proximal extension of the clot. In some cases it may be necessary to ligate even as high as the inferior vena cava.⁹²

Thrombophlebitis is less frequently a source of pulmonary embolism than is phlebothrombosis because the associated inflammatory reaction organizes the clot and prevents its breaking off. However, if the thrombus extends proximally, the fresh clot may not be sufficiently adherent, and emboli may be broken off by the current of blood.⁹³ Therefore the same therapeutic measures as those used in phlebothrombosis should be considered. In addition, if the extremity is cold, painful, sweaty, pale or cyanotic, procaine block of the sympathetic ganglions is recommended for relief of arterial spasm.⁹⁴ Rarely is the associated spasm severe enough to cause gangrene.⁹⁵ Moreover, not all patients with thrombophlebitis have abnormal arterial constriction in the affected limb: some may have a warm limb with good color.⁹⁶

Lately there has been considerable interest in the use of anticoagulant agents for the prevention and treatment of intravascular thrombosis, but unless carefully controlled these agents may lead to severe hemorrhages.⁹⁷⁻¹⁰⁰ In spite of its high cost, heparin is probably still the anticoagulant of choice.¹⁰¹ Administered intravenously its action is immediate and may be controlled by varying or stopping its administration, by giving protamine or by transfusions of plasma or blood. Dicoumarin, on the other hand, although inexpensive and easily (orally) administered, has several disadvantages. Its action is delayed and unpredictable, and since it has no effective antidote, its control may be difficult.¹⁰¹

* * *

Considered in their wider aspects, diseases of the peripheral vessels should be of interest not only to the surgeon specializing in them, but also to the physician of general or internal medicine. This

is so because these affections may be the first or only sign of existing or impending damage in more vital organs that are supposed to be the primary concern of the internist.

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The treatment of phlebothrombosis has been confused by the desire to avoid the danger of embolization. This latter consideration is of so much greater importance that measures designed to prevent the separation of the thrombus, once it

has formed, must take precedence over therapeutic procedures against phlebothrombosis per se. Therefore, active or passive motion is contraindicated when it seems probable that thrombosis has occurred.⁷⁷ Moreover, rest, immobility, local heat and elevation of the limbs may be inadequate in preventing embolization.⁹¹ For these reasons a more positive approach, venous ligation, is recommended. It has been emphasized that unilateral ligation may not be sufficient, since the predisposing factors to phlebothrombosis operate generally, and quite often thrombosis is present in both legs.⁷⁹ Furthermore, embolization is more liable to occur from the less obviously involved (less symptomatic) limb. Finally, ligation should be performed high enough to preclude the possibility of embolization from proximal extension of the clot. In some cases it may be necessary to ligate even as high as the inferior vena cava.⁹²

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, MD, *Editor**

BENJAMIN CASTLEMAN, MD, *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 29261

PRESENTATION OF CASE

A sixty-year-old Cuban was referred to this hospital because of a persistent cough and a mediastinal tumor.

For years the patient had been bothered by a slight nonproductive cough. Three months before entry the cough became worse, particularly when the patient was lying down, and became productive of one to two teaspoonfuls of gray-white phlegm. At that time he developed "a tired feeling" in the upper sternum. A month later he had intermittent dull, burning pains beneath the sternum and in the upper left chest, which were unrelated to effort or position and seemed to radiate through to the left scapula. The pains gradually increased in frequency and became almost constant. Exertional dyspnea, unassociated with orthopnea, developed and gradually became worse. One month before entry the patient's voice became hoarse, but there was no dysphagia. There was no palpitation, ankle edema, cyanosis, bloody sputum or weight loss.

The family history was noncontributory. The patient's wife had never been pregnant. The patient denied a penile sore, gonorrhea or a skin rash. Seven years before admission he developed filariasis, characterized by fever, "large glands" in the groin and "white urine" from the left kidney. A biopsy of a groin node showed filaria. He was treated with "ice therapy," and the illness promptly cleared. Since that time the patient had found it necessary to travel in the New England states or Canada during the summer months to avoid relapses.

Physical examination disclosed a pale, sallow, somewhat dehydrated man who coughed frequently, producing frothy yellow sputum. The pupils were equal and reacted to light and accommodation. The neck veins were not distended. One examiner felt a tracheal tug. The cardiac apical impulse was felt 8 cm to the left of the mid-sternal line in the fourth interspace. The sounds

were of good quality, and no murmurs were heard. The second aortic sound was louder than the pulmonic; neither was accentuated. The lungs were clear; the abdomen was negative.

The blood pressure was 100 systolic, 60 diastolic, in both arms. The temperature, pulse and respirations were normal.

The hemoglobin was 12.8 gm., and the white-cell count 12,800, with 74 per cent neutrophils, 14 per cent lymphocytes and 12 per cent monocytes. The urine was normal. Blood Hinton and Wassermann tests done in dilution were repeatedly negative. The sputum did not contain acid-fast organisms on one examination. The nonprotein nitrogen was 24 mg per 100 cc, and the protein 71 gm. An electrocardiogram showed slight sinus arrhythmia, with an average rate of 80. The PR interval was 0.15 second. T₁ was low, and T₂ and T₃ upright. T₁ showed a slight late inversion. The QRS complex was slightly blurred.

A chest roentgenogram (Fig. 1) disclosed a rounded mass with fairly sharply defined borders in the region of the aortic knob and descending portion of the aortic arch. This mass was about 80 cm. in diameter and could not be separated from the shadow of the aorta. Pulsations were visible over it, but their amplitude was less than that of the heart beat. The heart was not increased in size or abnormal in shape. The visible portion of the aorta was not abnormal. The left bronchus was displaced downward and inward by the mass and was also somewhat narrowed, but not blocked. There was an area of dullness in the right upper lobe immediately lateral to the mass described. The character of the dull area suggested a localized atelectasis. The diaphragm was low on both sides, and its respiratory movements were limited. There was no evidence of air trapping. An angiogram, although correctly timed was unsatisfactory; the film taken at the time the opaque substance (Diodrast) passed through the aorta was blurred because of motion.

An operation was performed on the sixteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR WILLIAM B. BRIDG. This man had been quite well up to three months previous to admission, when he began to cough and show signs of bronchial irritation on the left. Certainly his symptoms did not indicate that he had heart disease, and examination of the heart confirmed this. The electrocardiogram was not conclusive concerning any particular cardiac disease.

A whole paragraph discusses filariasis, but I shall devote little time to this diagnosis, since I know practically nothing about it.

*On leave of absence

DR. TRACY B. MALLORY: Dr. Cordero, who is here, can perhaps tell us about it.

DR. BREED: I hope to hear from him. I do not believe, however, that filariasis produces anything of this nature in the upper mediastinum. At the moment, unless I hear something from someone who knows more about it than I do, I shall discard the whole question of filariasis.

It is interesting that one person felt a tracheal

says about the films. There is one thing that I wondered about, Why was he not bronchoscoped? The x-ray film showed a narrowing of the left bronchus but the patient was operated on before bronchoscopy was performed.

DR. GEORGE W. HOLMES: He had been bronchoscoped in Cuba.

DR. BREED: Did you have a report of the bronchoscopy in Cuba?

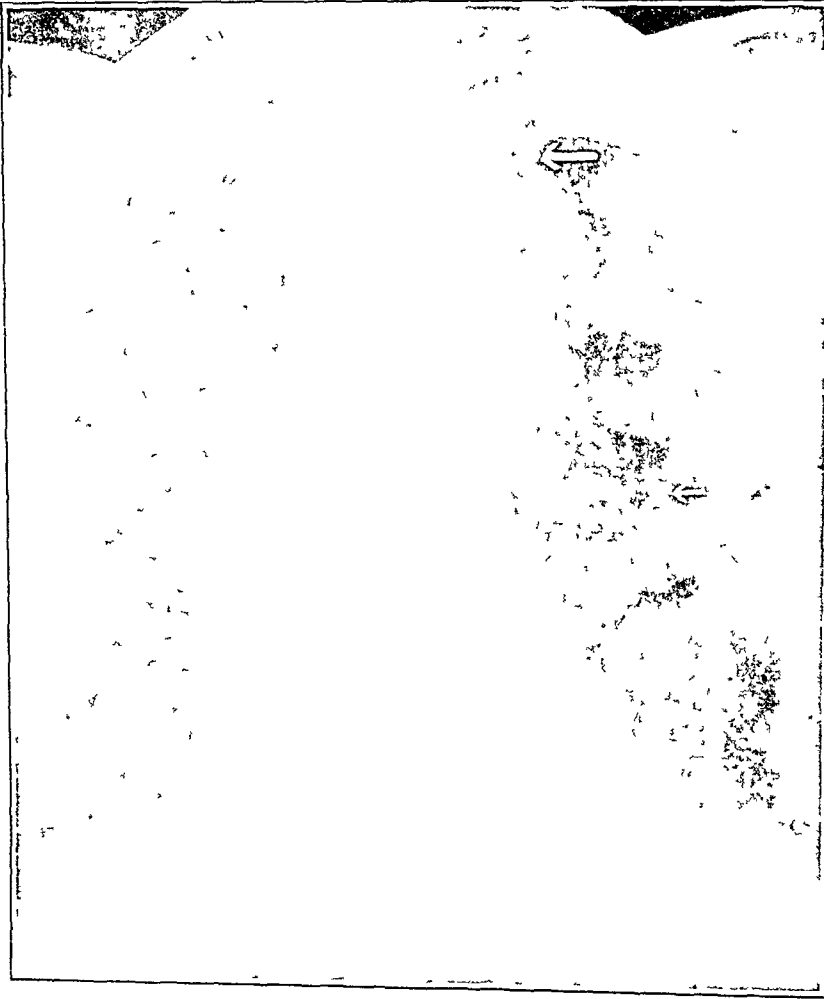


FIGURE 1. Roentgenogram of Chest.

The larger arrow points to the collapsed left upper lobe, and the smaller one to the residual lipiodol.

tug. I shall certainly not accept that if only one person felt it. It is a sign difficult to be sure of, and unless everybody felt it, it should not be accepted.

The blood showed a moderate degree of anemia but nothing characteristic. They did their best to obtain a positive Hinton test, having done many tests in dilution, but it was repeatedly negative.

We then come to the x-ray studies. The diagnosis depends almost entirely on what Dr. Holmes

DR. HOLMES: It was essentially negative.

DR. BREED: They found no narrowing of the left bronchus by bronchoscopy?

DR. HOLMES: No.

DR. BREED: The problem narrows down to whether he had a cystic or a solid tumor of the mediastinum or an aneurysm. I should like to ask one question before Dr. Holmes talks. Could an aneurysm of the aorta displace the left bronchus downward and inward?

DR. HOLMES: I think it could.

DR. BREED: I do not quite understand how, anatomically, an aneurysm of the aorta could displace the left bronchus downward and inward.

DR. RALPH ADAMS: The left primary bronchus comes out anterior to the aortic arch as it completes its turn posteriorly, so that mechanically it would be possible for an aneurysm of the antero-lateral surface of the arch of the aorta, just before it straightens out, to push the bronchus downward and inward.

DR. BREED: It may be mechanically possible, but I do not believe that I have ever seen an aneurysm of the aorta that displaced the bronchus in this fashion.

We have to consider a cystic or solid tumor arising somewhere in the mediastinum or from a bronchus. This man had some atelectasis of the left upper lobe. He may have had a carcinoma of the bronchus with a large metastatic lymph node. From the progress of the story, I am inclined to think that it was probably a malignant rather than a benign process. I should also like to ask if there was any accurate preoperative diagnosis put forward. I suspect they operated for diagnosis as well as treatment.

DR. HOLMES: This patient was carefully studied in Cuba by an excellent man, Dr. Pedro Finares, and I have some of his films here, as well as some of our own. He was referred to this hospital largely for treatment. They felt reasonably certain of the diagnosis. When we started to study the patient here we were unable to make a definite diagnosis. We eventually arrived at the same place that Dr. Breed has, namely, that this was either a tumor or aneurysm. Between what was done in Cuba and here, he had every possible test performed and we were still somewhat in doubt about the diagnosis.

DR. BREED: I still think that, if he had been bronchoscoped here, something might have been found.

DR. HOLMES: I do not believe so, and I shall tell you why in a moment.

This film was taken by Dr. Finares, after the injection of lipiodol. You can see the outline of the trachea at its bifurcation, this is the right descending bronchus, and here is the left descending bronchus. The mass lies in the angle between the bronchus and the trachea and has compressed the bronchus. If you look at the earlier films you notice an area of atelectasis in all the films. If the patient had a plugged bronchus it would be the bronchus leading to this area, and the bronchoscope would not reach that bronchus. Bronchoscopic examination, therefore, would be of no particular value.

This is the mass here. You can see it in the

lateral view, and we were never able to separate it from the aorta. This film was taken also by Dr. Finares and is a kymogram, a graphic method of showing whether or not pulsation is present. You do not have to rely on fluoroscopy. These lines represent the excursion of the heart or organ you are studying during the test. Over this area there is some excursion, not as marked as it is in the heart. We also have films over a considerable period of time, and there is a progressive increase in size, not by starts and stops. A portion of the lung is collapsed, and of course that is more likely to occur with a tumor that arises in and plugs a bronchus than with an aneurysm. An aneurysm can produce a collapsed lung, but it is only fair to say that an aneurysm of this size and position is unlikely to do so.

Then we tried taking over-exposed films to see if we could determine whether there was calcium in the walls of the tumor. The man had a negative Hinton test. So if it was an aneurysm it must have been on some basis other than syphilis. We were unable to demonstrate calcium. The heart was not enlarged. Not all cases of aneurysm have an enlarged heart, but a good many of them do, so that ought to help some.

Then we attempted to do a stunt that we thought would give us the answer—an arteriograph. The patient was willing to submit to it and the dye was injected into a vein. As you see, it first went to the right side of the heart; later it was in the pulmonary circulation; then a little later you see it in the left side of the heart. At that time it should have been in the great vessels and have given us the answer, but I was unable to interpret the findings. The film was not quite good enough, and the density of the dye was not great enough, possibly owing to the fact that it was injected too slowly. I think it is fair to say that the shadow of the tumor did not change appreciably in density, which it should have done if it were an aneurysm.

DR. BREED: This shadow looks almost continuous from the top of the heart.

DR. HOLMES: No; I do not believe that it is. We were not able to make a positive diagnosis, but we thought that this evidence was against aneurysm.

DR. BREED: Have you ever seen by x-ray a mass like this in the mediastinum representing a lymph node enlarged by metastasis from a bronchiogenic carcinoma?

DR. HOLMES: Yes.

DR. BREED: A small tumor with a large lymph node in this location is a perfectly good explanation?

DR. HOLMES: Yes.

DR. BREED: I am glad of that because that is what I should like to put as number one: an enlarged mediastinal lymph node caused by metastasis from a bronchiogenic carcinoma in the left upper bronchus. You have heard all the reasons. I do not believe that it was an aneurysm. In the first place if it were on an arteriosclerotic basis one would expect it to be calcified. The location is against its being syphilitic and, moreover, the Hinton test should have been positive.

DR. HOLMES: I might give one more clue. If it was an aneurysm, it was located in just the right place to produce a good tracheal tug.

DR. BREED: I do not believe that there was a tracheal tug. That statement was probably produced by the fervor of someone trying to make a diagnosis. Maybe he was backing an aneurysm. You have done that. Each of us has backed his own horse. If it was not a metastatic lymph node, I have not the foggiest notion what it was.

DR. MALLORY: Dr. Cordero, can filariasis be generalized enough to give mediastinal or pleural involvement?

DR. FERNANDO CORDERO: No. In the cases that we see in my country (Guatemala), the disease is cutaneous, with enlargement of only the superficial lymph nodes, especially the inguinal. We performed 60 or 70 autopsies on patients with filariasis and were unable to find any kind of microscopic lesions in the deeper tissues of the body, except for a few cases in which the infection had been present for five to ten years. In these, the tracheal lymph nodes were enlarged. Furthermore, all these cases of filariasis had characteristic blood changes. In 99 per cent an eosinophilia of at least 30 per cent was found. In this case eosinophilia was not present. Therefore I do not believe that it was filariasis.

DR. ADAMS: I should like to ask Dr. Holmes if he can state in which direction the trachea is displaced. It is to the right in the anteroposterior view. If he can make a positive statement regarding the displacement of the trachea in the lateral view, this might give a conclusive clue.

DR. BREED: I do not recall that the trachea was displaced.

DR. ADAMS: Am I correct in believing that the lower end of the trachea at the carina is displaced to the right in the lateral view?

DR. HOLMES: Yes.

DR. ADAMS: Is the trachea displaced in any other direction?

DR. HOLMES: What was said in the report?

DR. BREED: It did not say. No one said it was

displaced to the right in the report, but it obviously is.

DR. ADAMS: If the trachea were displaced anteriorly as well as laterally the mediastinal mass, to be an aneurysm, would have had to extend under it from a lateral origin, which it obviously does not do. Therefore, if the trachea is displaced anteriorly, I believe this must have been a carcinoma of the lung, as Dr. Breed has stated.

DR. HOLMES: I think the trachea is displaced anteriorly.

DR. ADAMS: It would be impossible for an aneurysm arising in the ascending aorta to displace the trachea anteriorly.

DR. HOLMES: That is an excellent point.

CLINICAL DIAGNOSIS

Aneurysm of aorta.

DR. BREED'S DIAGNOSIS

Carcinoma of left upper-lobe bronchus, with metastasis to mediastinal lymph node.

ANATOMICAL DIAGNOSIS

Bronchiogenic carcinoma of left upper lobe, with peribronchial and peritracheal metastases.

PATHOLOGICAL DISCUSSION

DR. MALLORY: There was a great deal of backing and filling on the part of all the people forced to attempt to make a diagnosis on this case. The patient was referred to Dr. Robert Linton, with the question whether it was an aneurysm that ought to be wired, and to Dr. Richard Sweet with the question whether it was a tumor that ought to be explored. It was evidently decided to explore, and Dr. Sweet operated. On opening the thorax, he came down upon a large mass of lymph nodes beside the trachea. He took a biopsy specimen, which showed frank carcinoma. Through this incision he was able to palpate the left upper lobe and found the primary tumor.

DR. HOLMES: One other statement that might be brought out now is that following the biopsy the patient was given 3000 r of million-volt x-ray therapy front and back, and you can see by comparing the first plate and the last one that there was no appreciable effect on the tumor. If we had used that as a therapeutic test we should have decided that it was an aneurysm.

DR. BREED: What was the x-ray diagnosis?

DR. HOLMES: I never was very positive. I believe that I was a little more in favor of aneurysm than of tumor. When you go back over them, there is enough evidence in the x-ray films to have made a correct diagnosis, but I did not do it.

CASE 29262

PRESENTATION OF CASE

A fifty-six-year-old laborer entered the hospital because of severe lower abdominal pain and constipation.

The patient was in good health, having never been severely ill, until twenty days before admission when, after no particular change in diet, he began to have severe low abdominal pain, referred chiefly to the left of and below the umbilicus. This pain continued in episodes of increasing severity. He then became constipated, being unable to have a bowel movement without a cathartic or enema. On one occasion he reported passing dark-red blood by rectum. He developed anorexia, and because of this the intake of foods and fluids had been markedly diminished. He had lost about 35 pounds during the present illness.

Six days prior to entry the lower abdominal pain and anorexia increased in severity. Thirty-six hours before admission the patient began to vomit; at first the vomitus was a bitter yellowish fluid but during the few hours before admission it changed to a foul-tasting, fecal-smelling, brownish material. He had taken little by mouth during the previous week and had had no results from enemas for several days, although he had continued to pass gas by rectum up to the time of admission. On the day of admission he vomited continually; this relieved the pain in the left lower quadrant for a few minutes, but it then came back in waves about four minutes apart. On the day of admission, the patient believed that his abdomen was larger than it had been.

The family and past histories were noncontributory.

Physical examination showed a tired, dehydrated, co-operative man who was obviously in distress from pain and repeated vomiting. The heart and lungs were normal. The abdomen was somewhat distended. Peristalsis was good, sometimes rushing, but the sounds were not high pitched. No masses were felt. There were tenderness and questionable spasm to deep palpation in the left lower quadrant. Palpation in this region caused pain all over the abdomen, especially in the right upper quadrant. After one examination, there was rushing peristalsis ending in fecal vomiting five minutes later. Rectal examination and proctoscopy for a distance of 35 cm. were not remarkable.

The blood pressure was 100 systolic, 85 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a red-cell count of 5,870,000, with a hemoglobin of 80 per

cent, and a white-cell count of 9900, with 85 per cent neutrophils. The urine was normal. One stool was guaiac negative.

A flat plate of the abdomen revealed several air-filled loops of small intestine that appeared slightly wider than usual. There were several areas of calcification measuring 1 cm. in diameter in the right midabdomen above the fifth transverse process.

When examined a few hours after admission the patient complained of abdominal pain, mostly paraumbilical and to the left, with pain in the back or shoulders and no abdominal discomfort or pain above the belt line. The abdomen was held in some voluntary spasm, but the right rectus muscle seemed tighter than the left. Tenderness was diffuse. Peristalsis was not particularly active except at five-minute periods, when he complained of colic. At these times, tinkles were heard but no rushes. The colic seemed to be paraumbilical and to move from left to right. The patient vomited fecal material, and a stomach tube produced 300 cc. of such material. A strenuous two-hour attempt to pass a Miller-Abbott tube through the pylorus was unsuccessful. At the end of this procedure the patient was tired out and the Miller-Abbott tube was replaced by a Levine tube.

Despite intravenous glucose and saline infusions and morphine, the patient grew more restless and the pain and vomiting occurred oftener. The pulse and respirations rose to 180 and 58 respectively and the temperature dropped to 97°F. approximately twelve hours after admission. The patient became slightly disoriented and deeply cyanotic, and the abdomen became quiet. The extremities were cold and clammy. The heart sounds were weak and of poor quality, and no blood pressure could be obtained. He died fourteen hours after admission.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD H. WALLACE: This patient had the classic symptoms of intestinal obstruction—abdominal cramps, fecal vomiting and obstipation. Colicky pain in the lower abdomen should have its origin in the large bowel, and with this, in a man of his age, pain and tenderness in the left lower quadrant are most commonly caused by diverticulitis of the sigmoid. The absence of a mass and no elevation of temperature or white-cell count should rule out this lesion, and in addition the x-ray films show no dilatation of the cecum or even an abnormal amount of gas anywhere in the colon. With such striking symptoms of intestinal obstruction these findings should eliminate the large bowel as the source of his trouble. The frequency of fecal vomiting greatly favors small-bowel obstruction, since, in general,

the rule holds—the higher the obstruction in the intestine the oftener the vomiting. Dilated loops of small bowel by x-ray substantiate the diagnosis of small-bowel obstruction.

We have no evidence to suggest inflammatory disease as a cause of obstruction and there is no history of previous operation, which might have caused adhesions. Externally there was no apparent hernia, which eliminates the commonest cause of small-bowel obstruction. The calcified areas shown by x-ray are presumably healed tuberculous nodes, and late obstruction might be caused by adhesions to one of these. An adherent Meckel's diverticulum is a rare cause of small-bowel obstruction, but complications from Meckel's diverticulum almost always occur before middle life. The history and sequence do not suggest regional ileitis. Intussusception can happen late in life and is usually associated with a polyp or benign tumor, such as lipoma, fibroma or leiomyoma. Indeed, these benign tumors may cause obstruction without this complication. Volvulus in the previously unexplored abdomen does not commonly occur in the colon, and much less so in the ileum or jejunum. Internal hernia occurs in various places and cannot be ruled out. The absence of a high white-cell count should rule out gangrene of the intestine or mesenteric thrombosis.

Foreign body is another possibility. It most commonly is a chicken bone, and one large enough to become stuck and cause obstruction. Such a bone might show by x-ray, but a fishbone or toothpick probably would not. Primary lymphoma of the bowel does occur and does advance to fatality without superficial nodal involvement, but in the advanced state a mass is usually palpable. Incidentally, a solitary lymphoma of the intestine should always be resected since it is sometimes a localized process that is not related to a generalized disease. Carcinoma of the small bowel can never be ruled out without careful barium studies, which in this patient were impossible.

The episode of pain, four hours before death, followed by diffuse tenderness, spasm and loss of peristalsis and then by circulatory collapse and death, suggests perforation of the bowel with massive peritoneal insult. I cannot make a diagnosis

of the cause of the obstruction but the likely possibilities are foreign body, carcinoma and lymphoma.

CLINICAL DIAGNOSES

Diverticulitis of sigmoid, with perforation.
Acute generalized peritonitis.

DR. WALLACE'S DIAGNOSES

Small-bowel obstruction, due to foreign body, carcinoma or lymphoma, with perforation.
Acute generalized peritonitis.

ANATOMICAL DIAGNOSES

Adenocarcinoma of transverse colon, with perforation.
Acute generalized peritonitis.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Dr. Wallace was correct in his diagnosis of perforation of the intestine with generalized peritonitis. The peritoneal cavity contained about 500 cc. of foul-smelling, creamy pus distributed from beneath the diaphragm to the pelvis. Some of the loops of small intestine were adherent to each other by strands of fibrin. The duodenum and jejunum were markedly dilated, but the ileum, cecum and ascending and transverse colons were not. The perforation was in a small annular constricting carcinoma of the transverse colon just proximal to the splenic flexure; it had already been almost completely sealed by the surrounding exudate. The presence of so much fibrin and frank pus and the partial sealing of the perforation indicate that the perforation had occurred before admission. Ordinarily an obstructing carcinoma in the region of the splenic flexure causes extreme dilatation and often perforation of the cecum. The fact that the cecum was not distended roentgenologically led Dr. Wallace away from a diagnosis of large-bowel obstruction. The right colon and ileum were almost certainly dilated before the perforation, but by the time the patient entered the hospital they had been decompressed by the perforation.

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AMERICAN MEDICAL ASSOCIATION

ALTHOUGH the annual scientific meeting of the American Medical Association was given up this year because of transportation and other difficulties resultant from the war, it is still necessary to conduct its affairs in an orderly manner. Therefore the House of Delegates was called together in Chicago on June 7, 8 and 9. This meeting was remarkable in that the attendance of delegates was approximately one hundred per cent. Every state delegation was filled, and every section delegate was present—only those from Alaska, Puerto Rico, Canal Zone, Philippines and Hawaii were absent. This is a truly remarkable

record in these difficult times, and a sure indication of how seriously the delegates respect their appointments.

Much routine business was transacted. Perhaps the most significant action was the setting up of the Council on Medical Service and Public Relations. This council is charged with the general consideration of all matters relating to medical service and their interpretation to the public. It will have the benefit of the work of both the Bureau of Medical Economics and the Bureau of Legal Medicine, and will be made up of one member from each of nine areas of the country so that it should well represent and amalgamate the great divergence of local opinion regarding such matters. To tie it in with the administration of the American Medical Association, the president, the immediate past president, the secretary and a representative of the Board of Trustees are members *ex-officio*. The House did not look with favor on the establishment of an office in Washington, D. C.

The Secretary reported an increase in membership of 2040 during the past year, in spite of the fact that a decrease had been predicted. In the last ten years the membership has grown from 97,111 to its present figure of 122,741. This growth is believed to be proportionately larger than the increase in the number of physicians in the United States and seems to refute the rumor that the American Medical Association is losing prestige among the physicians of the country.

The House was addressed by Surgeon General Kirk of the United States Army, who told about conditions in Africa and on other fronts, and General Grant, chief of the Air Medical Corps, told of the excellent training men in this arm of the service are receiving.

On Tuesday evening, Dr. Roger I. Lee, chairman of the Board of Trustees, presented the retiring president, Dr. Fred W. Rankin, with the President's Medal, following which the incoming president, Dr. James M. Paullin, of Atlanta, Georgia, was inducted into office. Much to the delight of the Massachusetts delegation, Dr. El-

liott P. Joslin was invested with the Distinguished Service Medal, which he accepted with his usual simplicity and grace. Dr. Paullin's address had to do with postwar conditions and was provocative of much thought. Dr. Herman L. Kretschmer, who has been treasurer for the past ten years, was made president-elect.

CONCERNING TROUSER CUFFS

A RECENTLY published pronouncement of the War Production Board in Washington has at last partly alleviated one of the more bizarre hardships of war. We may still go without tires, gasoline and sirloin steaks; we are still engrossed in the problem of keeping up with the changing styles in air-raid warning signals; we must pay taxes, buy bonds and shop unsuccessfully for that vanishing American, the potato; but we may again have cuffs on our pants. That is, if we are short enough, since a "32-inch waist regular" is allowed only a 35-inch inseam. So far as all recent advices are concerned, the restrictions on getting pants "on the cuff" remain the same.

The cuff restriction has already accomplished its main purpose, according to the WPB, since enough excess wool cloth has been recovered from 19,000,000 pairs of pants to make an extra 300,000 wool garments, also without cuffs. Such is the labor shortage, however, that it is still a grave question whether tailors can be found in sufficient numbers to sew together the amputated cuffs, like mink skins, in order to produce the extra 300,000 wool garments. Still later reports, this time from New Haven, indicate that the back rooms of tailor shops there are piled high with potential moth food—this mandatory material—awaiting some form of future usefulness. To a humble editor, it seems as if a more effective method of excess wool gathering would be the practice of collection at the source, like the less painful forms of taxation, rather than the making up so many million pairs of superfluously materialized pants, only to have this mass-scale *Schnitzenfest* to conform to the federal order.

Had we our hygienic-minded way with some of these affairs of greater or less importance, this sordid boon of turned-up pants would never have been granted even to the short men. In the first place, let short men recall that optical illusion by which cuffs on the pants, instead of an unbroken sweep of well-creased trousers, can make them look still shorter; and in the second place, let men of all stature remember trouser cuffs for the dirt traps that they are, and shun them hereafter and forever. True, trouser cuffs may have their uses, like catch basins, street gutters and grease traps, and many a time they have served as repositories for used matches, cigarette ashes and even burned-out butts by bashful youths caught smoking in a spotless parlor; but most of us prefer not to carry our dust bins as integral parts of our clothing.

MEDICAL EPONYM

WERLHOF'S DISEASE

The first reference to this syndrome was made by Paul Gottlieb Werlhof (1699-1767) in a footnote to his treatise "*De variolis et anthracibus* [Smallpox and Carbuncles]," published at Brunswick in 1735. The following is a translation of the passage in the third chapter of the essay, as printed in the second volume (page 539) of his posthumously collected works (*Opera Medica*, 1775-1776):

Might it not be supposed that these macules, having such an intimate association with hemorrhages, occur in conjunction with smallpox, not as a symptom but as a disease *sui generis*? I am led to this conclusion from having frequently observed this *morbus haemorrhagicus maculosus* in previously healthy persons without smallpox or any other acute disease either during the course of an intermittent fever or occasionally without fever. The pulse is at times small, quick and frequent (especially if there is a fever) and often irregular in force, and there is marked prostration until the macules gradually begin to fade, the bloody exudations cease and complete recovery ensues. For example, five years ago I saw this affection break out spontaneously in a ten-year-old girl, with profuse hemorrhages of foul or clear, black or serous blood from the nose, gums and throat, and in the vomitus, stools and urine, together with other variable symptoms, such as syncope and chills, while the macules, growing blacker and more abundant, gradually spread over the whole body. Although so much of the vital fluid had been lost that no strength seemed to be left in the pale, enfeebled body, nevertheless Nature with

the aid of my medicines fought, as Lucin says with all the blood that remained, and finally triumphed over the disease. After eleven days the spots disappeared, the hemorrhages ceased and there was gradual resumption of health, which has persisted up to the present time

R W B

DEATHS

CORIAT—ISADOR H. CORIAT, M.D., of Boston died May 26. He was in his sixty eighth year.

Dr Coriat received his degree from Tufts College Medical School in 1900, and later studied philosophy under William James at Harvard. From 1900 to 1905 he was a resident physician at the Worcester State Hospital from 1905 to 1919 a member of the neurological staff of the Boston City Hospital and from 1919 to 1928 consulting neurologist at the Chelsea Memorial and Beth Israel hospitals.

He was a trustee, librarian and chairman of the Educational Committee and an instructor of the Boston Psychoanalytic Institute. He founded the Boston Psychoanalytic Society, and was its president from 1930 to 1932. He had twice served as president of the American Psychoanalytical Association, once in 1924 and again in 1936. He was a member of the Massachusetts Medical Society and the American Medical Association.

ELLIOTT—ALFRED ELLIOTT, M.D., of Middleboro died March 1. He was in his seventy second year.

Dr Elliott received his degree from the College of Physicians and Surgeons of Baltimore in 1900. He served on the staff of St. Luke's Hospital. He was a member of the Massachusetts Medical Society and the American Medical Association.

RICHMOND—SIMON RICHMOND, M.D., of Boston died February 5. He was in his seventy first year.

Dr Richmond received his degree from Harvard Medical School in 1897. He was a member of the Massachusetts Medical Society and the American Medical Association.

YOUNG—ANNIE R. YOUNG, M.D., of Waltham died March 16. She was in her eightieth year.

Dr Young received her degree from Tufts College Medical School in 1911. She was a member of the Massachusetts Medical Society and the American Medical Association.

CORRESPONDENCE

SUPPLEMENTARY FOOD RATIONS

To the Editor Many physicians are puzzled by conflicting statements and lack of authoritative opinions on special rationing needs of the sick. Since these problems are faced by the medical staff of the Boston City Hospital in the care of outpatients and, at times, of discharged house patients the following plan was worked out for their guidance. It is presented here in the hope that it will be helpful to the profession at large.

The basic rations of processed foods (blue points) have been found intrinsically adequate in health as well as in disease. Practically, however, because fresh vegetables and fruit products are scarce or expensive, a few certificates have been issued for the always available and less expensive processed foods. The allowance has ranged from 8 to 20 pounds of processed foods, or up to 200 points per month. The average was 80 points per month.

On the other hand, several groups of patients need more of meat, fish, fats and cheese (red points) than is allowed by the basic ration. The most important are patients with diabetes, chronic gastrointestinal disorders (such as chronic ulcerative colitis, peptic ulcer and gastrointestinal resection), pernicious anemia, cirrhosis of the liver, hypoproteinemia and pregnancy. The average certificate issued was for 12 or 13 pounds of animal foods per month, 3 to 4 pounds in excess of the basic ration. Only an exceptional case required over 16 pounds. It is believed that 30 pounds of animal foods represents the absolute maximum that may be judiciously prescribed.

BOSTON CITY HOSPITAL
Ration Supplement Certificate

Date	194		
Name	(Record #)		
Address			
must have more foods than permitted by ration allowances. The following are necessary for months			
<u>Processed Foods</u>	<u>Meats</u>	<u>Fish</u>	<u>Fats and Cheese</u>
1b per month	Meats		1b per month
1b per month	Fish		1b per month
1b per month	Fats		1b per month
1b per month	Cheese		1b per month
1b per month			

Unrationed foods cannot be used because

Executive

Applicant may attach this certificate to CPA form #315

FIGURE 1

Most pregnant women and working or growing diabetic patients fall in this category. Unless great dependence is placed on the protein and fat of milk, all these patients need ration supplements. Controversy over the optimum fat intake of diabetic patients is the source of many of the conflicting opinions, but it seems fair to allow them to continue the diet to which they have become accustomed rather than to order substitution of unrationed commodities which may be restricted tomorrow. A table of the food requirements of such patients has been completed to assist the hospital staff in certifying ration needs (Table 1).

Many statements sent to rationing boards by physicians have been invalid because of failure to state that unrationed foods cannot be used with the reason why. A copy of the temporary form used by the Boston City Hospital, which satisfies all the present requirements of the OPA, is appended (Fig. 1). On the form, under "Processed Foods," the exact type must be specified. All unused spaces of the certificate are cancelled with an X. The hospital record contains a duplicate of this

TABLE 1. *Pounds of Food per Month Needed by Average Patients Eating Standard B. C. H. Diets.*

DIET	ANIMAL FOODS			PROCESSED FOODS ¹			
	MEAT — FISH	FATS	CHEESE	CANNED FRUIT	CANNED JUICES	CANNED VEGETABLES	CANNED SOUP
Diabetic:							
C 110, P 50, F 60 (1190 cal.) ²	6	4 (5)	—	0	4 ³	10 (25)	0
C 131, P 60, F 81 (1490 cal.) ..	7 (8)	5 (6)	—	0	4 ³	10 (25)	0
C 151, P 82, F 99 (1820 cal.).....	8 (10)	6 (7)	—	0	4 ³	11 (25)	—
C 172, P 95, F 121 (2160 cal.).....	8 (10)	6 (7)	2 (4)	0	4 ³	12 (25)	—
C 150, P 75, F 90 (1510 cal.).....	8 (10)	4 (6)	0	0	4 ³	8 (25)	—
With lunch box.....	12 (14)	2 (3)	—	0	4 ³	0 (25)	0
C 150, P 90, F 70 (1560 cal.).....	9 (12)	4	—	0	4 ³	8 (25)	0
C 200, P 110, F 90 (2050 cal.).....	12 (14)	4	2 (4)	0	4 ³	12 (25)	0
Pregnancy	12 (16)	2	1 (2)	—	8 ³	—	—
Gastric or duodenal ulcer.....	9 (12) ⁵	2	1 (2)	8 (10)	6 (10) ³	8 (10) ³	—
Colitis	8 (10)	4	—	8 (10)	— (5)	8 (10) ³	—
Chronic ulcerative colitis.....	12 (14) ⁵	4 ⁷	0	8 (10)	5	8 (10) ³	5
High-calorie (C250, P110, F120).....	10	2 ⁷	—	—	—	12 (25)	—
Liver disease (C300, P114, F50) ³	15 (30)	1	—	— (8)	—	8 (20)	—
Low-salt (P120).....	12 (14)	2 ⁷	2	—	—	12 (20)	—
Preoperative and postoperative ⁴	12	2	1	—	10	16	—
Hemorrhage ⁴	14 ⁵	2	1	5	5	8 ³	5
Acute illness (severe) ⁴	10	2	—	6	10	6	6
Pernicious anemia	7 ⁶	2	—	—	—	—	—

In the above table, the figures in parentheses are maximum and assume the use of foods with high ration-point values, that is. meat for protein, butter for fat and so forth; items listed "—" are not necessary but are not excluded; items listed "0" are excluded.

¹Specify exact type, such as pears, tomato juice, beans and chicken soup.

²Ordinarily no supplement is necessary.

³Limited to one month, and application must be signed by visiting physician.

⁴Limited to one month.

⁵Specify lean meat.

⁶Specify in addition pounds of liver customarily used by patient.

⁷Cream (unrationed) used in considerable amounts.

⁸Dependent on season.

statement, to which has been added the name of the prescribing physician and pertinent economic and medical data. National OPA regulations allow issuance of supplemental rations by local boards for only two months, but do not limit the duration of a certificate. Should a physician issue a certificate for a period longer than two

months it is, at present, up to the discretion of the local board to honor the request.

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NOTICES

AMERICAN CONGRESS OF PHYSICAL THERAPY

The twenty-second annual scientific and clinical session of the American Congress of Physical Therapy will be held September 8-11, at the Palmer House, Chicago. The annual instruction course will be held from 8:00 to 10:30 a.m., and from 1:00 to 2:00 p.m. during the days of September 8, 9 and 10, and will include a round-table discussion group from 9:00 to 10:30 a.m., Thursday, September 9. The scientific and clinical sessions will be given on the remaining portions of these days and evenings. A feature will be an hour demonstration showing technic from 5:00 to 6:00 p.m. during the days of September 8, 9 and 10. All these sessions will be open to members of the regular medical profession and their qualified aids.

For information concerning the instruction course and program of the convention proper, address the American Congress of Physical Therapy, 30 North Michigan Avenue, Chicago.

1943 GRADUATE FORTNIGHT

The 1943 Graduate Fortnight of the New York Academy of Medicine will be held from October 11 to 22. The current topic is "Disorders of the Digestive Tract."

There will be a carefully integrated program that will include morning panel discussions, afternoon hospital clinics, evening addresses and exhibits.

The following subjects will be included: the physiology of the gastrointestinal tract; emotions and gastric function; a critical review of gastroscopy; diagnosis and treatment of benign and malignant lesions of the stomach; the pathologic physiology of gastric and duodenal ulcer; recent advances in the therapy of peptic ulcer; disorders of the gastrointestinal tract in children; surgical aspects of congenital anomalies of the gastrointestinal tract in children; postcholecystectomy syndrome and its treatment; recent advances in the surgery of the pancreas; present status of regional enteritis and ulcerative colitis; the sulfonamides in gastrointestinal diseases; amebiasis and the flagellate diarrheas; problems of immunity to bacillary dysentery; the management of acute intestinal

(Notices continued on page xii)

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PHYSIOLOGIC CONSIDERATIONS IN THE TREATMENT OF NEPHRITIS*

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BOSTON

IT IS a very great honor for me to have been given this opportunity of presenting the fifty-fourth Shattuck Lecture. As you well know, this lectureship was founded in the year 1854 by a gift from the estate of George C. Shattuck, the elder, son of Benjamin Shattuck, a medical practitioner in Templeton, Massachusetts, and father of George C. Shattuck, the younger, the fourth Hersey Professor of the Theory and Practice of Physic. In earlier years at Harvard College it was the custom for all newly appointed professors to deliver an oration on taking office, and I feel that my lecture this evening corresponds in many ways to that earlier custom. With this in mind, I have selected a subject for discussion that has been of particular interest to several former professors of the theory and practice of physic. As the result of their observations we have obtained a clear picture of the pathologic changes that occur in nephritis and a good understanding of its clinical course.

This evening I wish to discuss particularly a rational basis for the treatment of the metabolic disturbances that occur in patients with renal insufficiency. Patients with kidney disease constitute a large and important group in both private and hospital practice. In the past it has been the custom to discuss therapy largely on the basis of the type of renal lesion. Such an approach usually resulted in prolonged discussion as to the nature of the renal disease and in little consideration for the specific correction or improvement of the presenting metabolic disturbances. A brief survey of the paragraphs relating to therapy in nephritis as recorded in standard medical textbooks is sufficient to impress one with the confusion that exists at present in this field. Medical students and house

officers are not infrequently bewildered as to how to proceed in attempting to correct the physiochemical disturbances that occur in patients with nephritis.

Contact with the clinical manifestations of renal disease soon impresses one with the fact that nearly every type of metabolic disturbance that is known to occur in conjunction with renal disease may occur in the presence of any specific type of renal lesion, although, as we know, particular metabolic disturbances are encountered with much greater frequency in association with certain types of renal lesions. This consideration might lead one to suspect that it would prove to be simpler and certainly more helpful if therapy were dictated primarily by the nature of the metabolic disturbance rather than by the type of pathologic change in the kidney. Thus the measures used in combating azotemia would be determined by such facts as whether azotemia was associated with dehydration, hypoproteinemia, edema or hypertension rather than whether azotemia was a consequence of acute nephritis, chronic glomerular nephritis, pyelonephritis or congenital cystic disease of the kidneys. We have a precedent for this approach in the methods employed in the treatment of diabetic acidosis and coma. In this disease hyperglycemia, acidosis, dehydration and lipemia are treated as such, and in outlining therapy little attention is given to the nature of the underlying pathologic changes. On the whole these patients do well because we have developed some degree of skill in estimating the *quantity* as well as the *quality* or type of therapeutic agents employed. Quantitative considerations play an extremely important role in the treatment of the metabolic disturbances associated with nephritis, since the body under these circumstances is so limited in its ability to compensate for an excess or deficiency of the indicated therapeutic agents. Hence it is not

*The Shattuck Lecture delivered at the annual meeting of the Massachusetts Medical Society, Boston, May 25, 1943.

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enough to know *what to use*—one must also have a very clear idea as to *how much to use!*

At this time it might be helpful to review a few basic physiologic principles, a knowledge of

TABLE 1. *Basic Dietary Requirements for Health.*

Water, sufficient to provide a urine volume of approximately 1000 cc daily
Calories, sufficient to maintain weight
Protein, approximately 1 gm per kilogram per day
Essential minerals and vitamins

which is essential to the intelligent application of the therapeutic measures indicated in the treatment of patients with nephritis. We know that

1 gm. per kilogram daily is adequate. Evidences of specific amino acid deficiencies may appear on diets of lower protein content unless the particular proteins used are complete in essential amino acids. The daily requirements for the various minerals and vitamins have now been fairly well established.¹

Since these four basic dietary requirements are the minimum necessary under optimal conditions, there is every reason to believe that in the presence of disease they will certainly not be decreased; in fact, the requirement of certain of them may be greatly increased. Hence there is little justification for a therapeutic regimen in the treatment of patients with renal insufficiency that permits

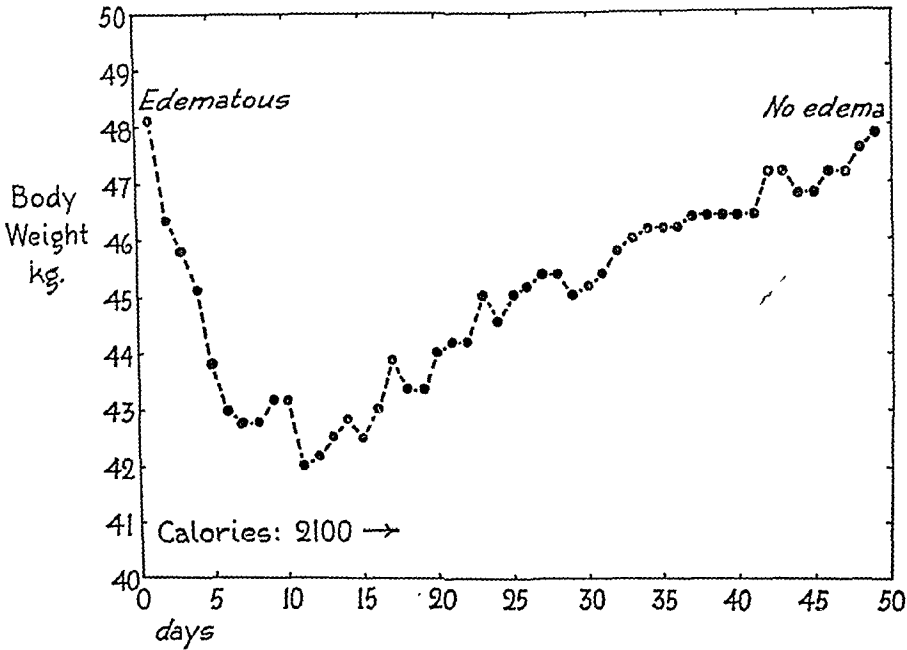


FIGURE 1. *Weight Curve in a Patient with Glomerular Nephritis.*

in order to maintain health the body must be provided with at least the four essentials (Table 1).

Under most conditions if water intake is sufficient to provide for a urine volume of 1000 cc. daily, renal function may be carried on quite satisfactorily. It is obvious that in the presence of renal insufficiency more water may be required than under normal conditions, since the kidneys' ability to concentrate urine may be markedly impaired.

The ideal diet for health is one that provides sufficient calories for maintenance of optimum weight. In undernourished patients, the caloric requirement will be considerably increased until optimum weight has been attained; in children, calories sufficient to permit normal growth must be provided. For adults, a protein allowance of

the exclusion or significant reduction in any one of these essentials for any continued period of time.

Difficulty in estimating the caloric requirement of patients with renal insufficiency. In health one can readily establish the caloric requirement of a subject by following changes in body weight in response to the ingestion of a diet of varying caloric content. In childhood, the added factor of growth must be considered. In most diseases the caloric requirement can also be estimated from changes in body weight. There are, however, at least two groups of diseases that provide notable exceptions to this rule: diseases associated with impaired intestinal absorption, that is, enteritis, sprue, cirrhosis of the liver and so forth; and cardiac and renal failure with edema.

In the first group of diseases weight loss may occur despite a normal caloric intake because of poor or impaired absorption from the gastrointestinal tract. In the second group weight gain may occur despite an inadequate caloric intake because of excessive salt and water retention. Thus in patients with nephritis it is frequently impossible to estimate the adequacy of caloric intake by following changes in body weight. This is well illustrated by the marked fluctuations in body weight that were observed in a patient with glomerular nephritis who was maintained on a constant diet of adequate caloric intake (Fig. 1). The patient had been ill for approximately ten days before entering the hospital. On admission this patient weighed 48.2 kg. and was markedly edematous. His daily caloric intake was 2100 calories. During the first ten days after admission a weight loss of over 6 kg. (approximately 13 lb.) was observed. This occurred despite the intake of adequate calories for weight maintenance. On the tenth day there was no edema present, and the patient appeared distinctly undernourished. Forty days later this patient weighed 48 kg., a gain of 13 lb. on the same caloric intake, that is, 2100 calories daily, and at that time there was no edema present. Thus on a constant diet adequate for growth this patient first lost weight, then gained, the loss being occasioned by excretion of fluid; the gain in this instance was largely new tissue.

Estimation of water balance. Because edema and dehydration are frequent complications of nephritis, considerable emphasis is placed on measurement of water balance. Unfortunately, to most physicians the term "water balance" indicates

TABLE 2 *Determination of Fluid Balance*

INTAKE	OUTPUT
Liquids	Urine
Water content of solid food	Feces
Water resulting from oxidation of protein, carbohydrate and fat	Intensible water loss
	Perspiration
	Abnormal water losses (saliva, sputum, draining fistulas and so forth)

simply the relation that exists between the quantity of liquids ingested and urine output! It is obvious from a study of Tables 2, 3, 4 and 5 that one cannot interpret water balance on the basis of the difference between fluid intake and urine output. Fortunately there are fairly reliable clinical signs that indicate changes in water balance, that is, increasing edema, dry skin, dry tongue, enophthalmos and so forth since under most circumstances it is impossible or impractical to make the elaborate measurements necessary for accurate determination of water balance.

In relation to edema it is important to emphasize the fact that the retention of additional fluid in the extracellular compartment is almost totally dependent on the retention of sodium.² Thus, it

TABLE 3 *Determination of Sensible and Insensible Water Loss (overnight weight loss under standard conditions).*

Weight of patient at 9 p.m.	52.5 kg
Weight of patient at 9 a.m.	52.2 kg
Difference	0.3 kg
$0.3 \text{ kg} \times \frac{24}{12} = 0.6 \text{ kg}$ insensible water loss in a 24 hour period	

may be stated that without a source of sodium there can be little retention of ingested fluid. This can easily be proved by drinking a large quantity

TABLE 4 *Calculation of Water of Oxidation*

1 gm protein	= 0.4 gm water
1 gm carbohydrate	= 0.6 gm water
1 gm fat	= 1.0 gm water
<i>Example</i>	
Diet Protein 70 gm	carbohydrate 200 gm
fat 120 gm	
$70 \times 0.4 = 28 \text{ gm}$	
$200 \times 0.6 = 120 \text{ gm}$	
$120 \times 1.0 = 120 \text{ gm}$	
Total	268 gm water

of water and restricting sodium chloride to 15 gm. or less per day. On this regimen little or no increase in body weight will be observed. If, on the other hand, one drinks adequate quantities of water and ingests large quantities of salt, excessive weight gain will occur and edema may become apparent. For the patient with nephritis it is well to emphasize the fact that quantities of sodium chloride as small as 2 to 5 gm. daily may present a tremendous excess for renal excretion and thus

TABLE 5 *Calculation of Fluid Balance*

Diet Protein 70 gm	carbohydrate 200 gm	fat 120 gm	
INTAKE			OUTPUT
Fluids	1500 cc	Urine volume	1150 cc
Water content of solid foods	600 cc	Fecal loss	250 cc
Water of oxidation	268 cc	Intensible water loss	792 cc
Total	2368 cc	Total	2192 cc
Difference between water intake (2368 cc) and water output (2192 cc) = 176 cc			
Weight of patient at beginning and end of 24 hour period revealed a gain of 0.1 kg (100 cc)			

induce an effect equivalent to 20 to 30 gm. of sodium chloride daily in normal subjects.

A factor that also may affect water balance in female patients with nephritis is the salt-and-water retention that occurs normally during the three to seven days prior to the onset of menstruation.³

Normal women are known to retain excessive quantities of salt and water during the week immediately preceding the onset of menstruation (Fig. 2). With the onset of menstruation, a diuresis is frequently observed and the excess fluid is eliminated. Female patients with nephritis may

ciently as can normal subjects, since the ability of the kidney to form ammonia from urea may be limited. Sodium and other fixed bases are drawn from the body and excreted in order to help neutralize acid end products excreted by the kidney. This may result in a severe depletion of the alkali

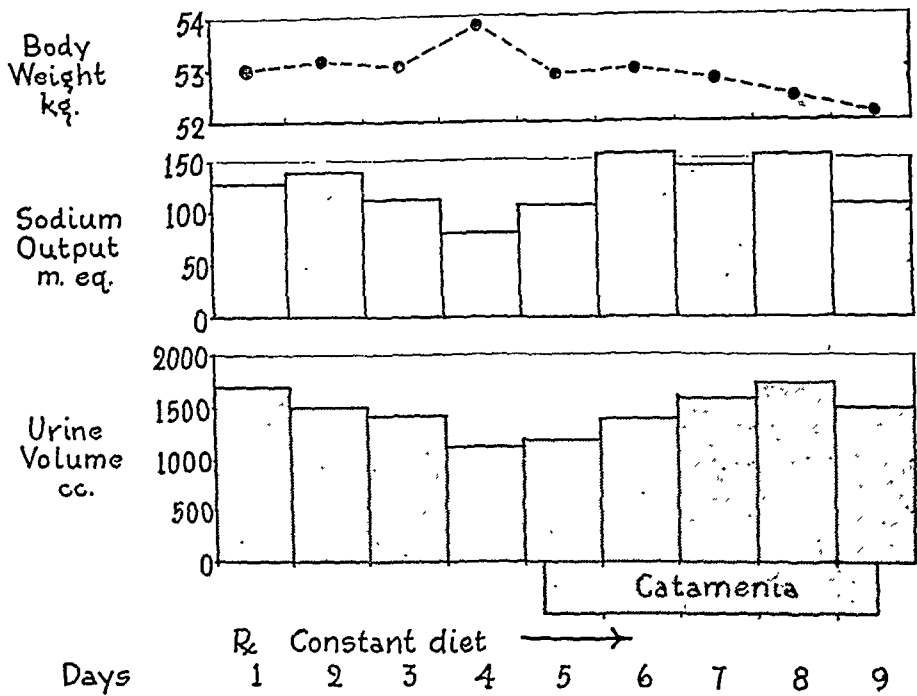


FIGURE 2. The Normal Premenstrual Gain in Weight Associated with Sodium Retention.

be expected to exhibit this same phenomenon during the years of ovarian activity. In the presence of a fundamental derangement that predisposes to fluid accumulation such as nephritis, however, one may expect a much greater total retention of sodium, chloride and water. Female patients afflicted with chronic nephritis have been suspected not infrequently of having recurrent exacerbations of their disease, as evidenced by the appearance of edema and a moderate rise in blood pressure during the phase of premenstrual retention of sodium, chloride and water (Fig. 3).

Acid-base balance. In normal subjects an equilibrium exists in which the acid ash of the diet and the acid end products of metabolism are eliminated with the use of a minimum quantity of fixed base—principally sodium. This is accomplished in part by the ability of the lungs to ventilate carbon dioxide, in part by the ability of the kidneys to form the base ammonia from urea, which is a waste product, and in part by the ability of the kidneys to eliminate an acid urine in the presence of a glomerular filtrate that is alkaline in reaction (Table 6). Patients with nephritis, however, can no longer conserve base as effi-

ciently as can normal subjects, since the production of acid metabolites cannot be decreased significantly in patients with renal disease who are resting in bed and who do not have fever, only two approaches

TABLE 6. Acid-Base Balance.

The body must be prepared to care for an excess of acid resulting from:	
End products of metabolism	
Acid-ash diet	
Several mechanisms are utilized in caring for an excess of acid:	
Buffer system of the blood	
Ventilation of carbon dioxide	
Excretion of an acid urine	
Formation of ammonia by the kidney	

are open by which one may conserve the base reserves of the body: decreasing the acid ash of diet by ingesting a diet of neutral or alkaline ash composition; and administering an excess of alkali (preferably sodium) to provide for the increased renal needs of fixed base. The former approach may be employed at all times; the latter is usually contraindicated in the presence of edema.

Aluminum hydroxide may be added to milk or taken with food; by so doing a great reduction

in phosphorus absorption can be demonstrated (Fig. 4). By employing aluminum hydroxide one is able to use foods of high nutritive value—for example milk—that naturally contain large quan-

and the serum carbon dioxide combining power gives one a fairly accurate indication of the serum base under most circumstances and permits one to decide whether sodium chloride or sodium bi-

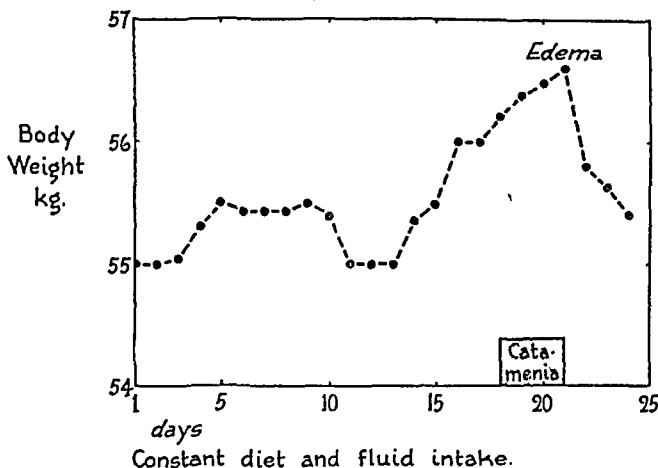


FIGURE 3. Changes in Weight during the Menstrual Cycle in a Nephritic Patient.

ties of fixed acid, and that without the addition of aluminum hydroxide, would add to the burden placed on the kidney.

Acid-base composition of blood plasma. Detailed analysis of the changes in acid-base composition of blood plasma that may occur in patients with renal disease has been presented by Peters and his co-workers.⁴ The physiologic implications that arise in relation to these changes have been clearly outlined by Gamble.² It is obvious that in the treatment of patients with renal insufficiency, just as in the treatment of patients with severe diabetes, one must have available laboratory facilities for certain chemical determinations. It is essential to limit the necessary determinations to those that can be carried out in most general hospital laboratories if the application of successful treatment is not to be limited to a few research centers. It would appear desirable to be able to determine the blood urea nitrogen or nonprotein nitrogen level of the blood, the total serum protein, the serum chloride and the serum carbon dioxide combining power. The albumin-globulin ratio is not essential for guiding therapy, since it is safe to assume that all patients with nephritis probably have some reduction in serum albumin level. A knowledge of the serum chloride level

carbonate or both should be administered or withheld (Fig. 5). In summary, one should be able to guide therapy efficiently and effectively in most cases if the following chemical determinations can be performed promptly: blood urea nitrogen or nonprotein nitrogen, total protein, serum chloride and serum carbon dioxide combining power.

Role of serum protein. An understanding of the composition and role of the serum proteins is essential in considering the treatment of patients with nephritis. The relation of albumin to globulin in the serum is well known, and the changes in colloid osmotic pressure that occur with changes in the relative quantities of these two proteins are evident (Fig. 6). A striking reduction in serum colloid osmotic pressure may occur in the presence of a normal total serum protein level as a consequence of a decrease in the albumin-globulin ratio. This latter change may be observed frequently in patients with acute nephritis in whom a rise in globulin frequently conceals a reduction in albumin. Thus despite a normal total serum protein level one may have a greatly reduced serum colloid osmotic pressure.

Longcope's⁵ studies have revealed that patients with acute nephritis of severe degree usually have a striking reduction in serum albumin level and a

corresponding rise in serum globulin. Patients with less severe renal damage show similar but less striking changes. Recovery from acute nephritis is usually associated with a rise in serum albu-

min. Since in most cases it is not possible to obtain a striking increase in serum albumin level with high-protein feeding or amino acids by mouth or intravenously, it is apparent that serum albumin

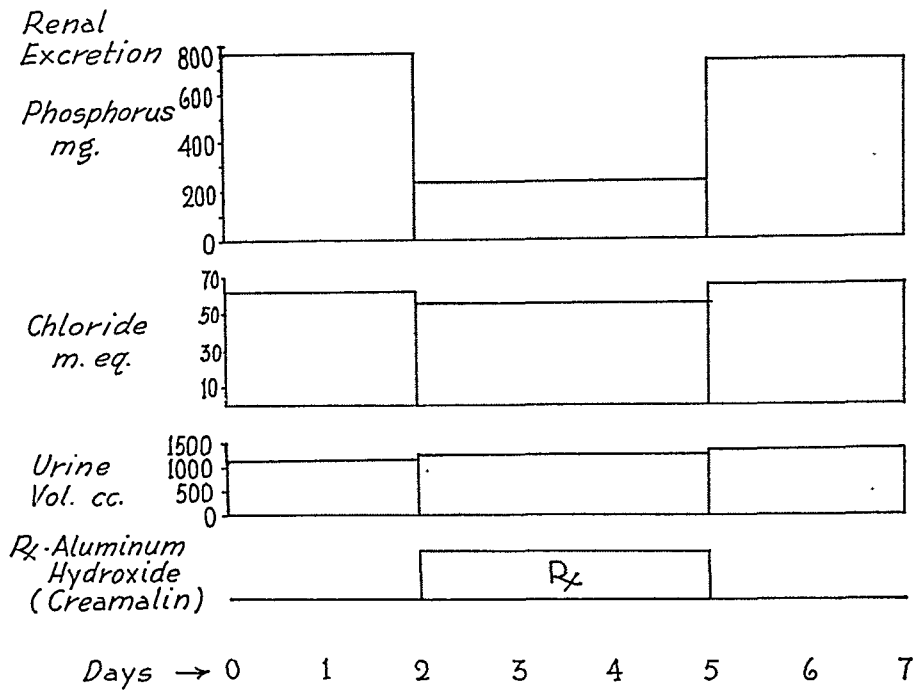


FIGURE 4. The Effect of Aluminum Hydroxide Therapy, Diet Being Constant.

min and a fall in serum globulin. It therefore appears that most patients with renal impairment,

administration is the only effective means of compensating for this deficiency.

Because of its apparent rapid utilization, serum albumin administration in doses available for chemical use should not be expected to increase the level of serum albumin. It can be estimated from studies on animals fed protein-deficient diets that in man an increase of 1 gm. in the concentra-

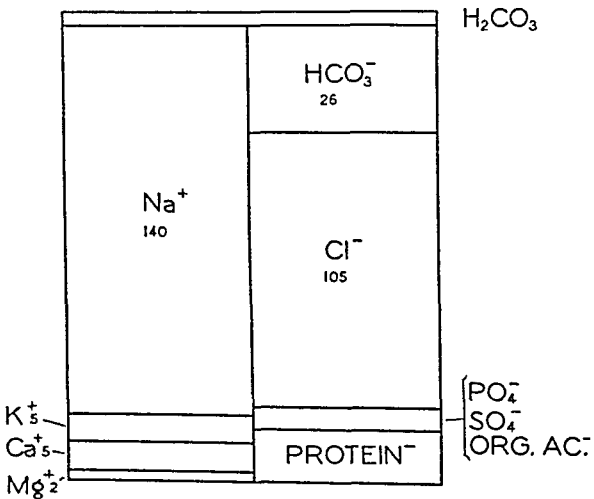


FIGURE 5. The Acid-Base Composition of Blood Plasma.

either acute or chronic, manifest some degree of serum albumin depletion, and therefore one of the most characteristic disturbances in metabolism associated with renal disease is hypoalbuminemia.

tion of serum albumin or a total increase of 30 gm. in plasma albumin on the basis of a plasma volume of 3000 cc. (Table 7) may be reflected in the entire body as necessitating the retention of 750 gm. of protein (Fig. 7).⁶ The concept that an equilibrium exists between the body protein in general and serum albumin aids in understanding

TABLE 7. Calculation of the Total Quantity of Protein in Plasma.

Plasma volume	×	protein concentration (gm. per 100 cc.)	=	Total protein
100				
Example:				
3000	×	7.0 gm.	=	210 gm.,
100				
of which two thirds is albumin, that is, 140 gm.				

why it is difficult, if not impossible, to increase appreciably the serum albumin level with the quantities of intravenous protein that can be given safely.

In administering protein intravenously to patients with renal insufficiency it appears that the

large dose in patients with hypertension or in patients with cardiac enlargement. It is possible, as a result of the reduction in edema and azotemia that frequently follows the administration of parenteral fluids and albumin solution, that the digestion and absorption of ingested protein and

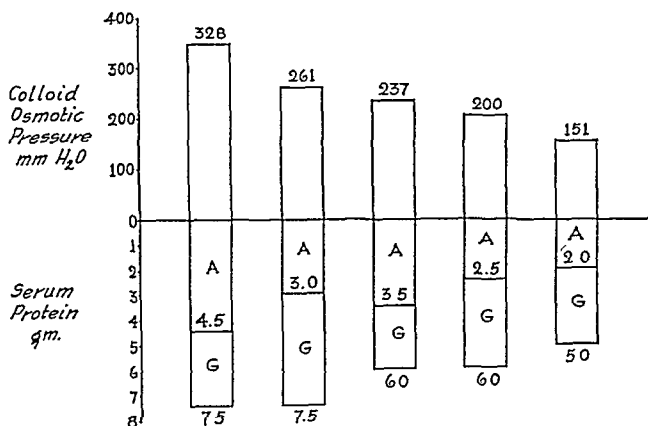


FIGURE 6. Serum Proteins and Colloid Osmotic Pressure.

chief benefit is derived from the temporary increase in colloid osmotic pressure, the resulting in-

crease in the synthesis of serum albumin from ingested protein may be improved, and this improvement in

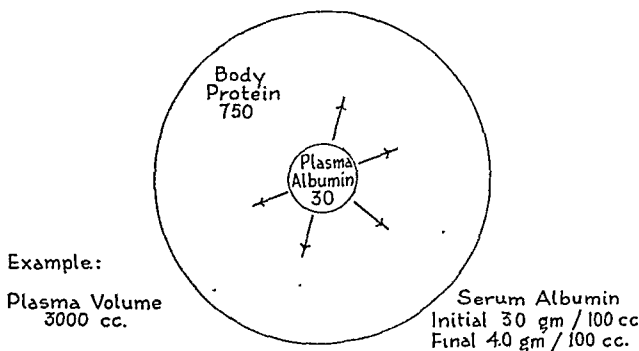


FIGURE 7. Diagram Showing That to Increase Serum Albumin 1 Gm. Requires the Retention of 750 Gm. of Protein.

creased hydremia, the increased glomerular filtra-turn may be reflected by a gradual rise in serum tion and hence the decrease in edema and azo-protein concentration. The total plasma content of protein may also play an important physiologic role. We are accustomed to assume that a value of 7 gm. of serum protein today and a similar value observed one or

two weeks hence represent equivalent quantities of serum protein in the body. Actually this may not be the case, since plasma volume may have increased or decreased in the meantime, and thus there may have been a considerable increase or decrease in the *total quantity of plasma protein*. This can be demonstrated by injecting slowly a measured quantity of serum albumin intravenously, under which circumstance little or no rise in serum albumin level will occur, but a very great increase in plasma volume can be demonstrated⁷ and of course the total quantity of plasma protein is temporarily increased. That such changes might occur spontaneously in patients with renal insufficiency is possible. It is of interest to note how frequently diuresis attended by no increase in serum albumin level is assumed to indicate that no change in serum protein could have occurred. Such a deduction is obviously subject to error unless plasma-volume measurements show that no change has occurred in the total quantity of serum albumin. In the absence of direct blood-volume measurement, changes in the red-cell count or hemoglobin may be useful in interpreting sudden changes in plasma volume. The determination of the albumin-globulin ratio may also be helpful in deciding whether a significant change in serum albumin has occurred.

To maintain nitrogen balance and to attempt to increase the serum albumin level one might consider the use of one or more of the following nitrogen-containing preparations: protein by mouth, amino acid by mouth, amino acid by vein, albumin intravenously, plasma intravenously and whole blood intravenously.

Adequate protein by mouth is of course indicated in all patients who are not nauseated or vomiting. Patients with renal insufficiency with normal blood-urea level may be given 2 to 3 gm. of

TABLE 8. *Some Advantages Pertaining to the Use of a High-Protein Diet in Patients with Renal Insufficiency associated with Edema without Azotemia or Acidosis.*

Improved nitrogen balance
Increased urea
Increased renal blood flow
Acid ash

protein per kilogram of body weight with advantage. In these patients a high-protein diet may be considered to be advantageous for several reasons (Table 8). Patients with elevated blood urea nitrogen will do better on a diet restricted to 0.5 to 1.0 gm. of protein per kilogram of body weight.

The oral administration of amino acid solution, a form of nitrogen that can be readily absorbed and that does not place so great a burden on the diges-

tive system as do the complex proteins, has been recommended for patients with renal insufficiency. Most patients, however, prefer complete proteins to the amino acid solutions that are available at present. Amino acid solutions by vein do not provide the colloid osmotic effect of protein solutions. Although amino acid solutions do form a ready source of nitrogen, and do represent complete replacement, there is little indication for their use in patients with renal insufficiency if albumin or plasma solutions are available. If parenteral therapy must provide all nutritional requirements for a period longer than one week, certainly the administration of amino acid solutions is indicated.

At present a solution of albumin has two advantages over a solution of concentrated plasma for patients with renal insufficiency: it can be prepared with a relatively low sodium chloride content, and it has a higher colloid osmotic pressure. Transfusions of whole blood provide hemoglobin in addition to plasma proteins and are the only effective treatment for the anemia so frequently associated with renal azotemia.

In the treatment of patients with azotemia without edema, it is generally recognized that forcing fluids is particularly advantageous in reducing the accumulation of metabolites in the blood. Many investigators believe that maximum glomerular filtration can be obtained if adequate quantities of water are ingested. Studies in dogs, however, reveal the fact that the rate of urine flow and the glomerular filtration (creatinine clearance) can be appreciably increased over the maximum obtained by fluid administration by mouth if glucose solution is administered intravenously. Further increases can be obtained if normal saline infusions are employed instead of glucose (Fig. 8). Until proved otherwise, it would appear to be advantageous to use these solutions parenterally in patients with azotemia without edema or impending cardiac failure.

Nausea and vomiting constitute a major complication in the treatment of patients with renal impairment. Under these circumstances all fluid and nourishment must be given parenterally (Table 9). It may be possible to administer water

TABLE 9. *Parenteral Therapy Required in the Presence of Nausea and Vomiting.*

Daily body needs.	
Water	2500 cc.
Calories	1200
Protein	25-50 gm.

by rectum; otherwise fluids and nourishment must be given intravenously or subcutaneously (Table 10). Under these circumstances one may attempt

to fulfill basic nutritional requirements by administering glucose and protein parenterally (Table 11). The provision of 1000 to 1200 calories and 25

dium and chloride, a decrease in the plasma volume and consequently dehydration and an *increase* in azotemia. Thus there is a real necessity for

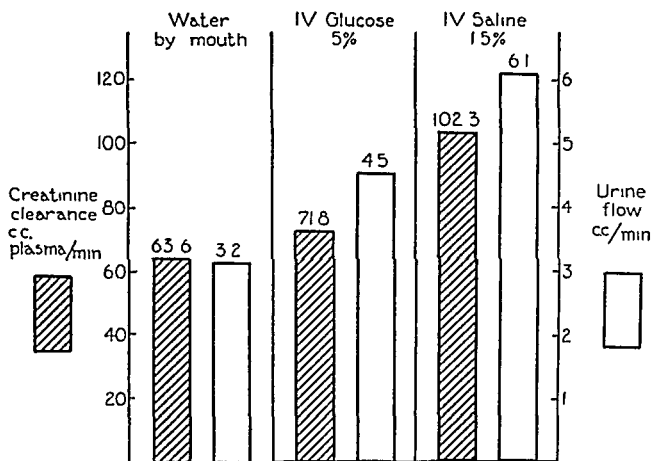


FIGURE 8 The Effect of the Intravenous Administration of Glucose and Saline Solution on Glomerular Filtration in Normal Dogs

to 50 gm. of protein may be considered to meet minimum basic requirements under these circumstances. Vitamin preparations may be given parenterally. Because of the large quantity of glu

providing sodium chloride, in small quantities at least, during such periods of active diuresis

General considerations. The commoner disorders that occur in conjunction with renal insufficiency are summarized in Table 12. It is obvious that solutions containing sodium and chloride might prove advantageous in the treatment of the first group of disorders (nausea and vomiting, azotemia and dehydration), whereas saline solutions would be contraindicated in most cases in the second group (edema, hypertension and cardiac failure). It is also obvious that whereas a high-protein intake might be advantageous to patients

TABLE 10 Nutritional Requirements in the Presence of Nausea and Vomiting

Water	Per rectum subcutaneously and intravenously	Glucose solution saline solution and lactate solutions
Calories and protein	Subcutaneously Intravenously	5 per cent glucose solution Glucose solution whole blood plasma or amino acids

cose solution needed, water requirements are easily met. *Glucose administration intravenously should not exceed a rate of 1 gm. per kilogram of body weight per hour* for optimum utilization. Hypertonic glucose solutions and protein solutions should be given very slowly and in small quantities to patients with hypertension, cardiac enlargement or acute nephritis.

When fluids are forced, either by mouth or parenterally, in the treatment of patients with azotemia, it must be recognized that essential minerals, such as sodium and chloride, are also lost in excess. Continued treatment of this type may result in a striking fall in the serum level of so-

TABLE 11 Basic Nutritional Requirements

Minimum daily caloric requirement	1000
Calories from 50 gm. of protein (4×50)	2000
Difference	1000
250 gm. of glucose is needed to provide 1000 calories. Therefore the administration of 2500 cc. of 10 per cent glucose solution will supply the necessary calories.	

with edema and hypoproteinemia, such a diet would be contraindicated in the presence of azotemia. Improvement can be expected in all cases, however, if glomerular filtration can be increased without placing too great a load on the heart. Disturbances such as those observed in calcium

and phosphorus metabolism, creatinine and uric acid have not been discussed individually since, for the most part, they are corrected when glomerular filtration is improved. It is to be noted that no

TABLE 12. *Commoner Disorders accompanying Renal Insufficiency.*

Anorexia, nausea and vomiting
Azotemia
Acidosis, dehydration
Anemia
Edema
Hypoalbuminemia
Hypertension
Cardiac failure

reference has been made to the type of nephritis or renal insufficiency with which the metabolic disorder is associated. This has been purposeful since, with rare exceptions, treatment based on correcting the presenting metabolic disorders will not be altered by the type of underlying renal disease.

With these considerations in mind, one can now arrange a group of effective physiologic therapeutic agents for use in the treatment of the metabolic disorders associated with renal insufficiency (Table 13).

I believe that practically all that can be accomplished in correcting the metabolic disturbances that are associated with renal insufficiency can be accomplished by the use of these simple agents.

TABLE 13. *Physiologic Therapeutic Agents Used in the Treatment of Metabolic Disorders associated with Renal Insufficiency.*

Water
Minerals:
Sodium chloride
Sodium bicarbonate and sodium lactate
Aluminum hydroxide
Glucose solutions
Solutions containing protein:
Albumin
Plasma
Whole blood
A diet containing the basic nutritional requirements for health

The problem is to match correctly the disturbances in function with the proper quantity of the indicated agent. Although the extent and progress of the underlying renal disease is the ultimate factor in prognosis, proper therapy may provide time for healing to take place in patients with an acute process, and may rehabilitate for months and even years an appreciable number of patients suffering from the effect of extensive and permanent impairment of renal function.

An outline of therapy suggested by the physiologic needs required to correct the metabolic disturbances that present themselves in patients with

renal disease follows. It is not to be presumed that these suggestions present all the effective forms of therapy or necessarily the most effective means of therapy; the outline is presented principally because it is based on physiologic considerations that should indicate appropriate measures.

Metabolic disturbances frequently associated with renal insufficiency. The treatment as outlined is based on the requirements of adolescents and adults. The same principles apply to the treatment of infants and small children, although quantitative requirements may differ appreciably and the administration of parenteral fluids will present greater practical difficulties.

GROUP I

1. *Edema.*

Purpose of treatment: Since in most cases edema is associated with hypoalbuminemia, therapy is directed toward increasing the colloid osmotic pressure of the serum, thereby increasing the plasma volume and aiding in the renal elimination of excess salt and water. A diet of acid-ash residue facilitates sodium loss and hence further reduces the quantity of extracellular fluid.

A. In absence of nausea and vomiting:

1. Diet, *salt free, high protein* (2-3 gm. per kilogram of body weight).
2. Fluids, 1500-2000 cc. by mouth daily.
3. Albumin,* 25 gm. intravenously daily. Plasma is less advantageous because of its high sodium chloride content. Ammonium chloride, mercurial diuretics, thyroid and urea may prove helpful but are not necessary if albumin is available for intravenous use.

B. In presence of nausea and vomiting:

1. Glucose solution, 1500-2000 cc. 10 per cent intravenously daily.
2. Protein (preferably albumin), 25-50 gm. intravenously daily.

The changes in body weight in a patient (P. B. B. H. M62053), a white man, 26 years of age, with a nephrotic syndrome of 3 years' duration, which followed the administration of albumin intravenously are presented in Figure 9. This patient had been bedridden for several months prior to the institution of albumin therapy and had failed to improve following treatment with a low-salt diet, high-protein intake, urea administration, occasional injections of mercurials and so forth, although on previous hospital admissions he had responded favorably to these therapeutic measures. It cannot be stated that albumin

*The human albumin used in this study was provided for experimental purposes through the courtesy of Dr. Edwin J. Cohn, Dr. Charles A. Janeway, Dr. Sam T. Gibson and Dr. Lorande M. Woodruff, of the Harvard Medical School. Albumin will not be available for general clinical use during the war because of the needs of the armed forces.

therapy intravenously was responsible for his improvement on this occasion. It can be stated, however, that this patient did present a marked albumin deficiency, and that parenteral administration of albumin solution was a sound method of compensating for the hypoproteinemia.

4. Venesection in presence of increased venous pressure.
5. Intravenous administration of fluids and protein solutions is *contraindicated*. Small

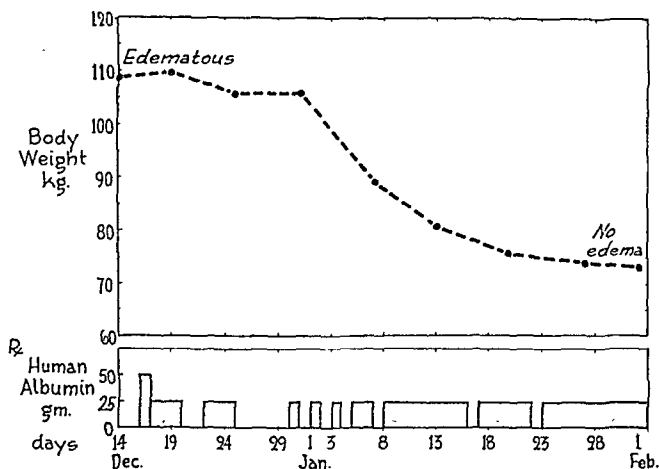


FIGURE 9. *Changes in Weight in a Patient with the Nephrotic Syndrome.*

2. Edema plus Hypertension.

Purpose of treatment. To increase the colloid osmotic pressure of the serum and at the same time to prevent overtaxing the heart.

- A. In absence of nausea and vomiting:
 1. Diet, *salt free, high protein* (2-3 gm. per kilogram of body weight).
 2. Fluids, 1500-2000 cc. by *mouth* daily.
 3. Albumin, 25 gm. in *divided doses* intravenously daily.
- B. In presence of nausea and vomiting:
 1. Glucose solution, 500 cc. 10 per cent intravenously every 6-8 hours.
 2. Protein (preferably albumin) 8 gm. intravenously every 6-8 hours.

3. *Edema plus Hypertension plus Cardiac Failure.*

Purpose of treatment. To improve the cardiac status and to facilitate the renal excretion of salt and water.

1. Diet, 1000-1500 cc. milk or fruit juice daily.
2. No additional fluids.
3. Digitalis and oxygen therapy.

quantities of hypertonic glucose solution—that is, 50 cc. of 20 per cent glucose—may be given on evidence of improvement in cardiac status.

4. *Edema plus Acidosis.*

Purpose of treatment. To increase the colloid osmotic pressure of the serum and to provide a relative excess of base.

- A. In absence of nausea and vomiting:
 1. Diet, 2000-3000 cc. milk daily, with added aluminum hydroxide, or an alkaline-ash diet of relatively high protein content.
 2. No additional fluids if milk diet is employed, otherwise fluids limited to 2000 cc. daily.
 3. Albumin, 25-50 gm. intravenously daily.
- B. In presence of nausea and vomiting:
 1. Glucose solution, 1500 cc. 10 per cent intravenously daily.
 2. Sodium lactate solution, 300 cc. 1/6 molar intravenously daily.
 3. Albumin, 25-50 gm. intravenously daily.

If sodium lactic is available in concentrated form (lactic acid *U.S.P.*), 4 cc. (equiva-

lent to 40 cc. 1/6 molar sodium lactate) can be added directly to the glucose solution to advantage, thereby decreasing the total volume of fluid.

5. *Edema plus Acidosis plus Azotemia.*

Purpose of treatment. To increase the colloid osmotic pressure of the serum, to increase glomerular filtration, and hence facilitate the excretion of sodium, chloride, water and end products of metabolism, and to provide a relative excess of base.

A. In absence of nausea and vomiting:

1. Diet, 2000-3000 cc. milk daily, with added aluminum hydroxide.
2. No additional fluids.
3. Protein (preferably albumin), 25 gm. intravenously daily for 3-7 days.
4. Glucose solution, 50 cc. 20 per cent intravenously for 3-7 days.
5. If satisfactory diuresis occurs and if edema disappears, give 300 cc. 0.85 per cent saline solution and 300 cc. 1/6 molar sodium lactate intravenously on every 3rd day that protein and glucose solution are given intravenously.

B. In presence of nausea and vomiting:

1. Protein (preferably albumin), 8 gm. every 8 hours.
2. Glucose solution, 750 cc. 10 per cent intravenously every 8 hours.
3. If edema disappears, give 300 cc. 0.85 per cent saline solution and 300 cc. 1/6 molar sodium lactate intravenously every 3rd day on the above regimen.

6. *Edema plus Acidosis plus Azotemia plus Hypertension.*

Purpose of treatment. To increase the colloid osmotic pressure of the serum, to increase glomerular filtration and at the same time to decrease azotemia, to provide a relative excess of base and to prevent overtaxing the heart.

A. In absence of nausea and vomiting:

1. Diet, 1500 cc. milk daily, with added aluminum hydroxide.
2. Glucose solution, 500 cc. 10 per cent intravenously once or twice daily. Albumin, 12 gm. intravenously once or twice daily.

B. In presence of nausea and vomiting:

1. Glucose solution, 2000 cc. 10 per cent intravenously in divided doses daily.

2. Sodium lactate solution, 300 cc. 1/6 molar intravenously in divided doses daily.
3. Albumin, 25 gm. intravenously in divided doses daily.

7. *Edema plus Acidosis plus Azotemia plus Hypertension plus Cardiac Failure.*

Purpose of treatment. To improve cardiac status and to provide a diet of low salt content, adequate protein, alkaline ash, adequate calories and minimum fluid.

1. Diet, 1000-1500 cc. milk daily, with added aluminum hydroxide.
2. No additional fluids.
3. Digitalis and oxygen therapy.
4. Venesection in presence of high venous pressure.
5. Administration of fluids and protein solution intravenously is contraindicated.

GROUP II

1. *Azotemia.*

Purpose of treatment. To increase glomerular filtration by providing an excess fluid intake; sodium chloride is given to increase plasma volume and to prevent salt depletion.

A. In absence of nausea and vomiting:

1. Diet with basic nutritional requirements.
2. Fluids, 3000-5000 cc. by mouth daily.
3. Glucose solution, 1000 cc. 5 per cent, or 500 cc. 10 per cent, intravenously once daily for 3-7 days.
4. Sodium chloride, 1-3 gm. (1 gm. enteric-coated tablets) daily in addition to usual salt in diet; after 1-2 weeks of observation it may be possible to increase the supplementary sodium chloride. Excessive gain in weight and development of edema are contraindications.

B. In presence of nausea and vomiting:

Day 1. Glucose solution, 3000 cc. 10 per cent, and saline solution 1000 cc. 0.85 per cent, intravenously daily.

Days 2 and 3. Glucose solution, 3000 cc. 10 per cent, and saline solution, 500 cc. 0.85 per cent, intravenously daily.

Day 4. If nausea and vomiting are not corrected, intravenous protein (plasma or albumin) 25 gm. must be given daily, in addition to the above.

A patient (P. B. B. H. M63653), a white man, 53 years of age, had had a unilateral nephrectomy performed for tumor of the left kidney. At that time, a hydronephrosis

of the right kidney had been demonstrated. Immediately following removal of the left kidney, the patient did well. 4 months later he was readmitted to the hospital because of nausea, vomiting, weight loss and weakness. At this time he was noted to have rather marked azotemia, the blood urea nitrogen being 78 mg per 100 cc (Table 14). Urinalysis revealed a low specific gravity, but otherwise was not remarkable. Phenolsulfonphthalein excretion was 7 per cent in 2 hours. Additional sodium chloride and

chloride and sodium bicarbonate under these circumstances may be nothing less than miraculous, and one may expect to rehabilitate such a patient for a period of 2 to 4 years. Since patients with a requirement of sodium chloride as great as this are very unusual, it is much safer to begin with small doses, that is, 1 to 3 gm daily. In the absence of excessive weight gain, cardiac enlargement or edema the quantity of supplementary sodium chloride may be slowly increased. During this

TABLE 14 Laboratory Data on a Patient with Hydronephrosis

DATE	BLOOD UREA NITROGEN mg/100 cc	SERUM CHLORIDE m eq/l	SERUM CO ₂ COMBINING POWER vol/cent	BLOOD PRESSURE mm Hg	URINE VOLUME cc	TREATMENT
February 18	78	103	33	180/105	?	Forced fluid and glucose intravenously
22	67	77	38	180/110	3500	As above
March 9	40	107	34	190/105	2000-3000	Sodium chloride (2 gm) and 1 mEq bicarbonate (1 gm) orally and glucose intravenously
April 7	2	114	51	165/110	2500	Sodium chloride (3 gm)

sodium bicarbonate were given on February 22 because the ingestion of large quantities of water by mouth and the administration of intravenous glucose in distilled water precipitated a striking reduction in serum chloride level. At present this patient is working full time and is being maintained on a daily diet that contains 50 to 60 gm of protein, 3000 to 4000 cc of fluids, 3 gm of sodium chloride and 3 gm of sodium bicarbonate.

2. Azotemia plus Acidosis

Purpose of treatment To increase glomerular filtration and to provide an excess of base.

A In absence of nausea and vomiting

- 1 Diet with basic nutritional requirements
- 2 Fluids, 3000-5000 cc by mouth daily
- 3 Glucose solution, 1000 cc 5 per cent, or 500 cc 10 per cent, intravenously once daily for 3-7 days
- 4 Sodium chloride, 1-3 gm by mouth daily in addition to usual salt in diet
- 5 Sodium bicarbonate, 3-6 gm daily by mouth, in presence of excessive weight gain or edema discontinue sodium chloride, if edema persists, reduce sodium bicarbonate

B In presence of nausea and vomiting

- Days 1, 2 and 3 Glucose solution, 3000 cc 10 per cent, saline solution, 500 cc 0.85 per cent, and sodium bicarbonate, 500 cc 1/6 molar, intravenously daily
- Day 4 If nausea and vomiting are not corrected, intravenous protein, 25 gm daily, must be given in addition to the above

Occasionally one encounters a patient with renal insufficiency in whom the sodium and chloride losses are so great that 10 to 15 gm of sodium chloride must be given daily. Such a patient may present the signs and symptoms of adrenal insufficiency. Response to sodium

period of treatment patients should be under rigid observation. In the presence of hypertension supplementary sodium chloride must be administered with great care.

3. Azotemia plus Hypertension

Purpose of treatment To increase glomerular filtration and at the same time to prevent overtaxing the heart.

A In absence of nausea and vomiting

- 1 Diet with basic nutritional requirements
- 2 Fluids, 3000 cc by mouth daily
- 3 Intravenous glucose solution, 50 cc 20 per cent, intravenously once daily for 3-7 days
- 4 Sodium chloride, 1-3 gm by mouth daily in addition to the usual salt in diet. *In the presence of hypertension the quantity of supplementary sodium chloride must be followed very carefully.*

B In presence of nausea and vomiting

- Days 1 and 2 Glucose solution, 3000 cc 10 per cent, intravenously, to be given slowly and in divided doses of not more than 1000 cc every 8 hours
- Day 3 Glucose solution, 2500 cc 10 per cent, and saline solution, 500 cc 0.85 per cent, intravenously daily
- Day 4 If nausea and vomiting are not corrected, intravenous protein, 25 gm daily in divided doses, should be given in addition to the above on alternate days

4. Azotemia plus Acidosis plus Hypertension

Purpose of treatment To increase glomerular filtration, to provide an excess of base,

and at the same time to prevent over-taxing the heart.

A. In absence of nausea and vomiting:

1. Diet with basic nutritional requirements.
2. Fluids, 3000 cc. by mouth daily.
3. Intravenous glucose solution, 50 cc. 20 per cent, intravenously once daily for 3-7 days.
4. Sodium bicarbonate, 3-6 gm. by mouth daily.

B. In presence of nausea and vomiting:

Days 1, 2 and 3. Glucose solution, and 2500 cc. 10 per cent, and sodium lactate, 500 cc. 1/6 molar, intravenously, *slowly* and in divided doses of 1000 cc. total every 8 hours.

Day 4. If nausea and vomiting are not corrected, intravenous protein, 25 gm. daily in *divided doses*, should be given in addition to the above.

5. Azotemia plus Hypoalbuminemia.

Purpose of treatment: To increase glomerular filtration, to increase serum albumin level without increasing nonprotein nitrogen level, and to prevent edema formation.

A. In absence of nausea and vomiting:

1. Diet with basic nutritional requirements, which includes 1 gm. of protein per kilogram of body weight.
2. Fluids, 2500-3000 cc. by mouth daily.
3. Protein, 25 gm. intravenously daily for 3-7 days.
4. Glucose solution, 500 cc. 10 per cent intravenously daily for 3-7 days.
5. Supplementary sodium chloride, 1-3 gm. daily, on and after the 4th day; in the presence of hypoalbuminemia the quantity of supplementary sodium chloride must be followed very carefully.

B. In presence of nausea and vomiting:

Days 1 and 2. Glucose solution, 2500 cc. 10 per cent, and protein, 25 gm. intravenously daily.

Day 3. Glucose solution, 2500 cc. 10 per cent, protein, 25 gm., and saline solution 500 cc. 0.85 per cent, intravenously daily.

Repeat the programs of Days 1, 2 and 3 in order until nausea and vomiting disappear.

6. Azotemia plus Hypoalbuminemia plus Edema

Purpose of treatment. To prevent the fluid that are used to increase glomerular filtration from accumulating in the body.

A. In absence of nausea and vomiting:

1. Diet, *salt free*; otherwise includes all basic nutritional requirements.
2. Fluids, 2000 cc. daily by mouth.
3. Protein, 25 gm. intravenously daily for 3-7 days.
4. Glucose solution, 50 cc. 20 per cent intravenously daily for 3-7 days.
5. If satisfactory diuresis occurs and if edema disappears, give 300 cc. 0.85 per cent saline solution, intravenously on every 3rd day that protein and glucose are given intravenously.

B. In presence of nausea and vomiting:

1. Protein (preferably albumin), 8 gm. intravenously every 8 hours.
2. Glucose solution, 750 cc. 10 per cent intravenously every 8 hours.
3. If edema disappears, 300 cc. 0.85 per cent saline solution is to be given intravenously every 3rd day on the above regimen.

A patient (P. B. B. H. M63459), a white boy of 14 years of age, was admitted to the hospital on January 31, 1943, with signs and symptoms of acute nephritis. His clinical course during the first three weeks in the hospital was complicated by middle-ear infection and an attack of rubella. His blood urea nitrogen slowly increased to 163 mg. per 100 cc., and on February 19 he was drowsy, nauseated, azotemic, acidotic, edematous and unable to retain fluid or food. It was apparent that intravenous administration of dextrose alone was not helping him; sodium chloride intravenously was contraindicated because of his edema. It appeared that the best form of treatment that could be administered under these circumstances would be small doses of albumin, glucose and lactate solution given intravenously in the hope that some improvement in glomerular filtration might occur as the result of the increase in plasma volume. The albumin was given in divided doses—that is, 12 gm. administered very slowly—and the heart and circulation were watched very carefully. The striking improvement that followed is of great interest (Table 15). It cannot, of course, be attributed necessarily to the treatment. On this regimen, however, it was possible to provide the patient's protein and caloric requirement, and there is no doubt that this was of value in a boy who was undernourished. Of particular interest was the fact that the administration of protein intravenously in the presence of azotemia was followed by a positive nitrogen balance and a decrease in blood urea level (Fig. 10). Again, of special note was the striking decrease in serum chloride level that followed the continued administration of albumin, glucose and lactate solution intravenously and that necessitated the administration of sodium chloride on February 27

and 28 (3 gm daily for 2 days (Table 15). At present (May 25) this boy is up and about and is being maintained on a diet of 80 gm of protein daily. The blood urea nitrogen is less than 20 mg per 100 cc

7. Azotemia plus Hypoalbuminemia plus Edema plus Acidosis.

Purpose of treatment: To prevent the fluids that are used to increase glomerular filtration from

4. Glucose solution, 50 cc. 20 per cent, intravenously daily for 3-7 days.
5. If satisfactory diuresis occurs and if edema disappears, give 300 cc. 0.85 per cent saline solution and 300 cc 1/6 molar sodium lactate intravenously on every 3rd day that protein and glucose solution are given intravenously.

TABLE 15 Laboratory Data on a Patient with Glomerular Nephritis

DATE	BLOOD UREA NITROGEN mg /100 cc	SERUM CHLORIDE m eq /l	SERUM CO ₂ COMBINING POWER vol /cent	BLOOD PRESSURE mm Hg	URINE VOLUME cc	TREATMENT
February 1	117	-	36	142/80	400	Glucose intravenously
4	128	-	-	140/85	1100	As above
10	160	-	-	138/92	1700	As above
13	157	103	38	-	1400	As above
19	163	101	38	134/98	860	As above
20	136	-	-	137/100	560	As above plus sodium lactate and albumin
23	128	85	48	150/90	1660	As above
26	108	85	40	150/114	960	As above plus supplementary salt
March 1	84	100	39	170/120	1330	Fluids by mouth
8	47	101	35	160/114	2630	As above
15	56	106	45	144/112	1640	As above
Apr 1 14	25	-	-	118/82	3300	As above

accumulating in the body and at the same time to provide for an increased quantity of available base.

B In presence of nausea and vomiting:

1. Protein (preferably albumin), 8 gm intravenously every 8 hours.

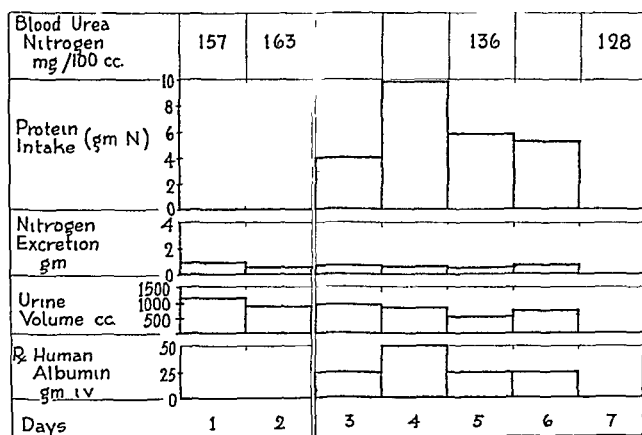


FIGURE 10 The Effect of Protein Therapy on the Nitrogen Balance and Blood Urea Nitrogen Level in a Patient with Glomerular Nephritis

A. In absence of nausea and vomiting

1. Diet, 2000-3000 cc milk daily, with added aluminum hydroxide
2. No additional fluids
3. Protein, 25 gm. intravenously daily for 3-7 days

2. Glucose solution, 750 cc. 10 per cent intravenously every 8 hours
3. If edema disappears, give 300 cc 0.85 per cent saline solution and 300 cc 1/6 molar sodium lactate intravenously every 3rd day on the above regimen

Recently Luetscher and Blackman⁹ have described the development of a peculiar serum electrolyte disturbance in patients with uremia that followed sulfonamide administration. In most cases patients were admitted to the hospital in uremic stupor with a history of having had a respiratory infection treated for several days with sulfonamide medication. In the hospital, therapy consisted of large quantities of glucose and saline solutions administered parenterally. With the onset of diuresis, the serum sodium and chloride, which had previously been low, rose to unusual heights, that is, serum chloride 140 milliequiv. per liter and serum sodium 170 milliequiv. per liter. It appeared that the peculiar renal disturbance associated with sulfonamide administration permitted the excretion of water in excess of sodium chloride. If this disturbance could be detected early, the administration of large quantities of fluid by mouth and glucose solution by vein—*with no sodium chloride*—should be effective in rapidly reducing the abnormally high serum levels of sodium and chloride. It is obvious that such disturbances can rarely be detected without the aid of repeated serum chloride and carbon dioxide determinations.

SUMMARY AND CONCLUSIONS

Much of the confusion that now surrounds the treatment of renal insufficiency might be obviated by adopting a simple, straightforward plan of therapy based on a careful consideration of the agents required to correct the principal disturbances in body chemistry and physiology, rather than by adopting a plan of therapy that is dictated by the nature of the pathologic lesion in the kidney. Such an approach will necessitate familiarity with the chemical and physiologic changes that may be expected to occur in the presence of impaired renal function.

In the outline of a therapeutic regimen designed to improve or correct the metabolic disorders that are associated with renal insufficiency, *quantitative* as well as qualitative considerations require attention, since patients with kidney disease are unable to compensate adequately for either an excess or a deficiency of the indicated therapeutic agents. The therapeutic agents that

are required in the treatment of renal insufficiency are few and for the most part represent merely replacement of normal body constituents. Hypoalbuminemia is one of the most characteristic metabolic changes associated with renal insufficiency, and there is a great need for an unlimited supply of albumin for parenteral administration if patients with renal insufficiency are to be treated adequately. A plan of therapy has been suggested for use in the treatment of the commoner disorders associated with renal impairment. The successful application of such a program requires constant and intelligent day-to-day supervision. It also requires the availability of facilities for the determination of blood nonprotein nitrogen, serum chloride and carbon-dioxide combining power. Although the progress and extent of the underlying pathologic process in the kidney is the ultimate factor in prognosis, proper therapy may provide an opportunity for healing to take place in patients with an acute or active process, and may rehabilitate for months and even years an appreciable number of patients incapacitated by the effects of extensive and permanent impairment in renal function.

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MENINGOCOCCAL MENINGITIS WITH PURULENT ARTHRITIS*

Report of a Case

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CASE REPORT

JOINT symptoms are not uncommonly associated with meningococcal meningitis and meningococcemia. Herrick and Parkhurst¹ refer to descriptions by the Massachusetts Medical Society as early as 1810, and Osler² notes an 1811 report of epidemic cerebrospinal fever by North in which "swelling like rheumatism in the joints" was described. Both papers give an excellent historical review of the subject.

No adequate statistical data on the incidence of such joint manifestations have appeared since the reviews of Herrick and Parkhurst¹ and Rolleston⁴ in 1919. In an analysis of 321 cases in an army camp, the former found a frequency of 4 to 7 per cent. Rolleston collected a series of 902 cases and noted an incidence of 65 per cent. The occurrence of purulent effusion necessitating aspiration is not well known. Among 502 cases of meningitis in the British Navy, Rolleston found 24 with arthritis but only 1 had sufficient fluid to necessitate aspiration. Herrick and Parkhurst¹ had 16 such cases out of 321 patients with meningitis.

Subsequent to these reviews, there is little more than an occasional case report of meningococcal arthritis until the appearance of a review of 23 cases by Schein⁶ in 1938. Fourteen of these are said to have had joint effusion, although the fluid was aspirated in only 6 cases. Hench, Bauer and their colleagues⁶⁻¹³ have published eight reviews covering the American and English literature of the past decade in a very thorough manner. The sections on meningococcal arthritis for the years 1939 and 1940 (the latest thus far published) report no purulent arthritis, and only a few cases were noted in the preceding years. Dingle et al.¹⁴ mentioned a case without effusion in 1941. Therefore, it may be justifiable to assume that meningococcal arthritis with purulent effusion is a rarity, and one would postulate that the incidence would be further diminished with sulfonamide therapy.

The case of meningitis with meningococcemia presented here is of interest because of the development of purulent arthritis after the institution of adequate sulfadiazine therapy.

A 52-year-old housewife (B C H 1050039) entered the hospital with chief complaints of confusion, joint pains and rash. She had been well until the evening of the 2nd day before admission. At that time she first complained of feeling chilly and displayed signs of mental confusion. The following day she noted generalized joint and muscle pains and a generalized red rash and developed a stiff neck. On the morning of admission she was further confused and was unable to recognize the members of her family, but did so following admission. The family and past histories were irrelevant.

Physical examination showed a well-developed and well-nourished white woman lying flat in bed in no acute distress when quiet, but crying out with pain on any motion whatsoever. The temperature was 101.2° F, the pulse 108, and the respirations 38. The patient was oriented as to time and place but sporadically confused concerning the details of her illness. Over her entire body there were petechiae that did not blanch on pressure and that varied in size from 1 to 4 mm in diameter, as well as petechiae of the bulbar conjunctivas and the buccal mucosa. There were also two 1-cm hemorrhagic blebs overlying a metacarpophalangeal joint on each hand. The tongue was coated, and the throat and conjunctivas were injected. The lungs were resonant to percussion and clear to auscultation. There was a slight enlargement of the heart to the left, the rhythm was regular, and there was a Grade 1 systolic murmur over the aortic area. Moderate voluntary spasm of the abdominal wall was noted, but rigors, localized spasm and tenderness were absent. The spleen and liver were not palpable.

The neck was extremely stiff. Brudzinksky's sign was present bilaterally but Kernig's sign was absent. The patient was lying with all joints of the extremities in semiflexion. Gentle, passive motion of fingers or forearms elicited screaming but attempts to bring out Kernig's sign met with little complaint. There was no swelling, heat or redness of any of the joints. The physical and neurologic examinations were otherwise negative.

On lumbar puncture there was an initial pressure of 250 mm of water. Gray, turbid fluid was removed in which there were 12,450 white cells per cubic millimeter, with 98 per cent polymorphonuclear leukocytes containing gram-negative, intracellular diplococci. The total protein was 366 mg per 100 cc and the chlorides 663 mg. The blood sugar was too low to be read. Admission spinal fluid blood and throat cultures were found to contain Group 1 meningococci. Blood studies showed a hemoglobin of 82 per cent (Sahli), 4,760,000 red cells and 16,150 white cells 75 per cent of which were neutrophils. The nonprotein nitrogen was 24 mg per 100 cc. The urine was negative except for a ++ test for albumin. A blood Hinton test was negative.

Shortly after admission 5 gm of sulfadiazine was given by elixir and in oral dose of 1 gm every 4 hours. The

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temperature began to drop soon after admission and by midnight reached 97°F. (rectal), the blood pressure being 85/62 and the pulse rising at times to 150. The patient did not appear to be in marked collapse, although on one occasion she was sweating profusely and the skin was cool. She was given 30 mg. of calcium pantothenate intramuscularly, and desoxycorticosterone was made readily available, in the event of frank signs of the Waterhouse-Friderichsen syndrome. This state of relative hypothermia and hypotension persisted essentially unchanged until noon of the 3rd day, when the rectal temperature rose, reaching 100.8°F. that night, and the blood pressure returned to normal limits.

Although the blood level of free sulfadiazine was 15.6 mg. per 100 cc. the morning following admission, the blood culture was still positive at that time, but it was negative on all succeeding occasions.

The petechial rash disappeared completely by the 3rd day, at which time a maculopapular, blanchable, extensor-distributed rash appeared over the buttocks, knees, elbows, thighs and pretibial regions, but not on the back or abdomen. These lesions caused much distress because of marked pruritus, but had disappeared by the 7th day.

On the 6th day, the patient complained of leg pains in addition to the aforementioned arthralgia, and both knees were found to be hot, swollen, slightly red and exquisitely tender. The following day, turbid fluid, which clotted almost immediately, was aspirated from both knees. It contained 39,400 white cells per cubic millimeter, with 98 per cent polymorphonuclear leukocytes; no organisms were seen in stained smears, and the fluid was sterile on culture. The free sulfadiazine level of this fluid was 8.6 mg. per 100 cc. Concomitant with the development of the joint effusions there appeared a cluster of eight punctate, hemorrhagic, herpetiform papules on the volar surface of the right forearm. They were nonblanchable and caused no discomfort. These lesions faded slowly and there was only a residual erythema on the 23rd day.

Subsequent lumbar taps were done, all fluids being sterile and chemically and cytologically showing a return toward normal. The last was performed on the 7th day and clear fluid was withdrawn, which was normal in all respects except for 340 white cells per cubic millimeter, with 98 per cent lymphocytes. The knees were aspirated on the 8th, 11th and 14th days, and each time sterile fluid without detectable microscopic organisms was obtained, except for the last tap, when only 0.5 cc. of fluid was available and no studies were possible. The other two samples contained 26,200 and 78,700 white cells per cubic millimeter respectively, of which 99 per cent and 100 per cent were polymorphonuclear leukocytes. On the 11th day, with the patient fasting, joint aspiration and venepuncture were performed concomitantly. The fasting blood sugar was 81 mg. per 100 cc., but the joint-fluid sugar level was too low to be read. The blood protein was 4.86 gm. per 100 cc., and the nonprotein nitrogen 22 mg. The respective joint-fluid levels were 4.70 gm. and 24 mg. per 100 cc. These joints showed much improvement clinically between the 11th and 14th days, as evidenced by decreased pain, tenderness, swelling and limitation of motion.

The joints of the upper extremities had been decreasingly painful on motion, but on the 9th day swelling, tenderness and increased limitation of motion occurred in the left elbow. This joint was not tapped and the reaction subsided concomitantly with that of the knees,

though motion was somewhat limited for several days. Heat and passive motion as well as active motion and sporadic splinting were applied therapeutically to the effusive joints. This resulted in almost complete return of function on discharge.

Throughout the first half of the hospital stay, the temperature was of a mildly septic variety, although there was only one spike as high as 103°F. (rectal), and the pulse varied between 80 and 110. The white-cell count ranged from 15,000 to 24,550, and the blood level of free sulfadiazine ranged from 6.0 to 11.0 mg. per 100 cc. The drug was omitted on the 10th day and low-grade temperature continued during the subsequent week, although the joint reaction was obviously subsiding. Sulfadiazine was reinstituted in a daily dosage of 6 gm. on the 17th day and continued for 1 week. At that time the temperature had been flat for 48 hours and the drug was omitted. The temperature remained essentially normal until the time of discharge on the 29th day, and the white-cell count ranged from 9000 to 11,000.

Throughout the course, the patient was oriented as to time and place and variably somnolent, depressed, alert and euphoric. The lungs were persistently clear on physical examination and the cardiac murmur did not change. An electrocardiogram showed only sinoauricular tachycardia (rate, 107). Repeated x-ray films of the chest were negative. Roentgenograms of both knees and both elbows on the 18th day revealed no abnormalities except minimal hypertrophic changes of the left knee.

At the time of discharge, the patient was able to move about with facility and without pain, tenderness or stiffness of any joints except the left elbow. This joint was painless although it was limited to 15° of full extension.

The patient came to the hospital for follow-up examination 3 weeks after discharge and was able to extend the left forearm fully. The temperature was normal and the patient was asymptomatic except for generalized weakness.

DISCUSSION

The points worth considering in this case are the presence of a positive blood culture sixteen hours after institution of sulfadiazine therapy, the appearance of three somewhat different types of skin lesions during the course of the illness and the development of purulent joint effusions five days after an adequate sulfadiazine blood level had been obtained.

In general, the value of sulfonamides in the treatment of meningococcal infections is widely recognized.^{10, 11, 14-19} Rapid, dramatic and uneventful recoveries have been noted in cases of acute and chronic meningococcemia and meningitis with and without joint involvement. An exception to this rule is reported as having occurred in a patient with meningitis and meningococcemia who, ten days after sulfadiazine therapy was established, had persistently spiking fever and purulent effusion into a knee joint.¹⁵ He had had no joint swelling on admission. The fluid was sterile on aspiration and the temperature and joint symp-

toms subsided gradually. The patient was essentially well three weeks after admission and was discharged.

The positive blood culture in the present case, in view of the blood level of free sulfadiazine (15.6 mg. per 100 cc.), is not consistent with published clinical observations. This fact was commented on by Dr. Maxwell Finland, who saw the patient in consultation. This finding suggests, perhaps, a relatively refractory strain of meningococcus. Such a phenomenon would explain the elevated temperature until somewhat late in the course of the illness, and the development of a septic focus not evident at the time of admission.

The rash noted on admission was petechial and typical of meningococcal septicemia. The second rash, a maculopapular, blanchable, extensor-distributed lesion appearing on the fourth hospital day, is characteristic of sulfonamide toxicity.²⁰⁻²³ It is also described by Herrick,²⁴ in association with joint effusion, as characteristic of meningococcal infection. Stott and Copeman¹⁰ note that there may be such a rash with or without a central, hemorrhagic area in chronic meningococcemia. This eruption was fading on the sixth hospital day, when the evidence of frank knee-joint effusion was first noted. However, the earliest clinical evidence of joint effusion may have been missed, since the polyarthralgia of admission was still present. The appearance of the third rash on the sixth day, a localized collection of eight punctate, herpetiform, hemorrhagic, lesions 2 mm. in diameter on the volar surface of the right forearm, was possibly associated with a sporadic bacteremia. The source of such a bacteremia could not be determined but might have been in the knees, although knee and blood cultures at that time were sterile.

In 1919, Herrick and Parkhurst¹ categorized the various joint phenomena associated with meningitic infection, and their classification has been generally adopted with few modifications.^{5, 7, 9, 25} Briefly, they suggest three groups. In *Type A* an acute polyarthritis appears as an initial or early symptom, coincident with the petechial rash, and is usually transitory. There is marked pain and tenderness on motion but little or no effusion, and the symptoms are attributed to hemorrhagic lesions of the joints and synovial structures. This type may be present or absent in a given case and may run into the second form, *Type B*. This usually occurs about the fifth day of the disease. It is usually monoarthritic, affecting a knee most commonly, and is characterized by signs of purulent effusion. The aspirated fluid is mucinous, purulent, hemorrhagic or any combination of these; it contains 1000 to innumerable leukocytes per cubic

millimeter, and meningococci are found by smear or culture or both in about one third of the cases. There is less spasm, pain and tenderness than one would expect from the appearance of the joint, and the signs usually last one to four weeks, with subsequent complete recovery. *Type C* refers to joint involvement associated with serum therapy, a type which is of little concern here. In a series of 321 cases of meningitis, Herrick and Parkhurst found 14 *Type A* and 16 *Type B* cases, although a review of the brief case reports they give leaves one in some doubt as to their rigidity in applying the criteria they set up. Autopsy data are not available on the cases that failed to recover.

Keefer, Parker and Myers²⁵ have described the gross and microscopic pathology of knee joints in 2 patients with meningococcal arthritis. The first patient, with a proved case of meningococcal meningitis, developed pain, tenderness and slight swelling of the left elbow on the thirteenth day of illness and died on the twenty-first day. The knees were opened for post-mortem examination, although the patient had never shown signs or symptoms of knee involvement. No evidence was found of bone or cartilage destruction, and there was an intact synovial surface layer. The deeper layers of the synovia, however, showed an acute inflammatory reaction and numerous gram-negative diplococci, mostly extracellular. In the second case, a patient with proved meningococcal meningitis, there was pain in both knees, and death on the third day of the disease. At autopsy, there was no excess of synovial fluid in the knee joints and the microscopic picture noted above was observed. However, in addition the surface layer of synovial cells was swollen, necrotic or entirely absent in some places, leaving a surface of granulation tissue and a thick layer of cellular exudate composed of polymorphonuclear leukocytes. There was no extension deep into the capsular tissue. In summary Keefer et al., note: "Meningococcal arthritis is a metastatic lesion involving first the deeper synovial tissues. Later, infection invades the superficial cells with effusion of fluid into the joint cavity and varying degrees of destruction of the cartilage. It is essentially a metastatic acute synovitis." If these tenets are correct, the criteria of Herrick and Parkhurst¹ of *Type A* as an early transitory, hemorrhagic polyarthritis and of *Type B* as a later, protracted monoarticular synovitis are incorrect and the typing is superfluous. However, more clinical data correlated with pathological findings are necessary before the classification can be justifiably dismissed. Herrick and Parkhurst's observation of exquisite tenderness of *Type A* joints and relatively few subjective signs in the

Type B group is not consistent with the pathology reported by Kcefer et al. The present case demonstrates no sharp line of demarcation between nonexudative and exudative arthropathy, and in the latter type of involvement the joints were very painful and quite consistent with their clinical appearance.

Comparable symptomatology in swollen joints is reported by Schein.⁵ He reviewed 23 cases of meningococcal infection with articular involvement, devoting emphasis to the generally good prognosis that Herrick and Parkhurst gave to such joints. Contrary to this, Schein found that many patients needed orthopedic treatment and 3 patients developed ankylosis. However, at least one of these, judging from the case descriptions, had only some stiffness and no ankylosis. Brinton²⁶ states that pain and disability are uncommon in meningococcal arthritis and that the inflammation involves the synovial membrane and is not associated with changes of the bone ends. Keefer and Spink²⁷ report that gonococcal arthritis, which is closely related to the meningococcal form, may cause fibrous, but seldom bony, ankylosis. The greater the amount of fluid that collects in the joint space, the less the chance of destruction, according to these authors. Therefore, large joints like the knee have a relatively better prognosis. The case reported in this paper bears out this thesis in that there was residual stiffness in the elbow for some time after the knees were functionally normal. There were essentially no joint symptoms three weeks after discharge.

In view of the inability to culture organisms from aspirated joint fluid on three different occasions, the pyrexia and the maculopapular rash, it was suggested that the symptoms might have been due to sulfadiazine toxicity. The literature referring to sulfatoxic arthritis is not extensive. Hench, Bauer et al.,¹⁰⁻¹³ Keefer,²² Finland et al.²⁰ and Spink and Hansen²³ in reviews of toxic manifestations of sulfonamides either mention transient arthralgias or do not include a section on joint symptoms. However, Long et al.²⁸ in such a review state: "Painful joints have been reported in the course of sulfanilamide therapy and we have noted several patients who have received sulfathiazole have had exquisitely tender, swollen joints. . . . [This] may be puzzling in gonorrhea because of the resemblance to gonorrheal arthritis." This paper has no bibliography. The only case of true joint effusion attributable to sulfonamide toxicity is that of Glicklich and Sherman,²¹ in which a patient developed effusion of both knee joints during sulfadiazine therapy. Fifty cubic centimeters of clear, serous, sterile fluid containing a few polymorphonuclear leukocytes was aspirat-

ed. The drug was omitted and the effusion subsided, but recurred when sulfadiazine was given again.

An attempt was made to differentiate sulfatoxic arthritis and meningococcal arthritis in the present case on the basis of cytology and chemistry of the aspirated synovial fluid. A number of informative studies on the clinical physiology and pathology of synovial fluid have been made by Ropes et al.,²⁹ Keefer et al.,^{27, 30} and Coggeshall et al.³¹ Judging by these reports, the fluid in the case presented here was definitely abnormal, having a high count of leukocytes, almost exclusively polymorphonuclear. According to Coggeshall,³¹ protein above 3.15 gm. per 100 cc., in synovial fluid is abnormal. Keefer and Spink²⁷ state that although a synovial-fluid sugar level markedly lower than the blood-sugar level in the fasting state does not necessarily mean an infected fluid, it is suggestive of one. The data on synovial fluid in the present case might obtain in any of a number of arthropathies but are most consistent with one of pyogenic etiology. However, no published material is available that enables one to state dogmatically that such findings could occur in sulfatoxic arthritis.

Therefore, although in a given case no definite etiologic conclusions can be drawn from the characteristics of joint fluid if it is sterile, it was believed on the basis of circumstantial evidence that the present case was one of meningococcal arthritis. After the sulfadiazine had been omitted for a week, it was reinstituted for seven days to rule out any possibility of sulfatoxic arthritis and there were no succeeding symptoms.

SUMMARY

A case of meningococcal meningitis with meningococcemia is presented, with the onset of purulent knee effusions six days after sulfadiazine therapy was begun.

The literature on the incidence, clinical types and pathology of meningococcal arthritis, as well as that of sulfatoxic arthritis, is briefly considered.

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MEDICAL PROGRESS

CLINICAL CATALYTIC CHEMISTRY

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IT IS the purpose of this report to call attention to the development of a field of laboratory medicine that has been emerging from many diverse sources in the past decade. This field has to do with biological catalysts. A generation ago, Otto Folin, D. D. Van Slyke, S. R. Benedict and others initiated a feverish study of metabolites that culminated in modern clinical chemistry. The metabolites studied—for example the blood sugar—are usually present in concentrations that may be described in milligrams of blood or tissue. Likewise, the daily excretions thereof are frequently measurable in grams or in sizable fractions of a gram-molecule. On the other hand, in recent years clinical studies have shifted more and more toward the description of specific catalysts, the concentrations and excretions of which are described in micrograms. This thousandfold change in parameters is the logical corollary of the nature of catalysts, in that biologic catalysts expedite the turnover of relatively large amounts of metabolite without contributing to the final product. For this reason, although subject to loss through

wear and tear and leakage, a little catalyst goes a long way.

The clinical measurement of these catalysts has a special significance for two reasons. In the first place, much more specific information is obtained and therefore the clinical interpretation is the more certain. For example, the blood urea may be elevated under many diverse circumstances and the interpretation of a high blood urea nitrogen value requires an intimate knowledge of the patient and his history. On the other hand, although an intimate understanding of the patient is still essential, an elevation of the so called plasma "hormonal iodine" is prima-facie evidence of hyperthyroidism.

In the second place, because catalysts control the rate of metabolic turnover, their concentration has a peculiarly dynamic significance. For example, a single determination of the blood sugar records, at best, an equilibrium in carbohydrate metabolism under the conditions prevailing. In contrast, the height of the plasma hormonal iodine reflects directly the rate of dynamic metabolic turnover. In a sense, these catalytic levels are direct-reading speedometers that indicate at any given moment how fast certain specific physiologic systems are operating. For this reason, they tend

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more and more to replace the cumbersome functional or tolerance tests now in vogue.

Another advantage of this trend is that the technic employed is often catalytic in nature. Consequently the methods represent advances in two respects. First, they require much less material. For example, the hormonal iodine can be determined in 1 cc. of plasma instead of 10 cc. as required by the older titration method. Secondly, the methods have become more specific. Thus, by selecting the proper strain of yeast, the influence of thiamine on fermentation can be used to estimate the amount of thiamine in a sample of biological material.

These microcatalytic methods require more precise attention to the time of reaction than did many of the older stoichiometric methods. They frequently require micromanometric apparatus or direct-reading colorimeters like the Klett-Summerson.¹ They demand also scrupulous attention to thermostatic control, because the rate of most biochemical reactions is significantly influenced by temperature. In general, these methods have been applied to the following types of substance: Hormones, vitamins, enzymes and electrolytes, including the hydrogen ion. The following examples illustrate some applications and certain precautions peculiar to these procedures.

HORMONES

In the case of hormones, two recent developments are of special interest, namely the application of iodide catalysis to the determination of plasma hormonal iodine, and the development of a new photometric technic for determining androgens and related 17-ketosteroids.

Determination of plasma hormonal iodine. This method is the outcome of physicochemical experiments by Sandell and Kolthoff² on the rate of reduction of ceric ions by arsenious acid. In its simplest terms the reaction may be expressed thus: (Yellow) $\text{Ce}^{+++} \rightarrow \text{Ce}^{++}$ (Colorless)

This reaction is markedly accelerated by iodide ions. Kolthoff and his co-workers studied the various conditions involved, including the concentration of total electrolyte and the temperature. Subsequently Chaney³ proposed adapting the method to the blood iodine.

Before the plasma is analyzed for iodine, it should be partitioned to separate the protein-bound from the inorganic iodine, as described by Salter.⁴ In this way, even accidental contamination with iodine during sampling or subsequent handling may be successfully eliminated. This treatment is conveniently carried out in graduated centrifuge tubes (15-cc. capacity). The reagents may be either

those of Bassett, Coons and Salter⁵ or those of Man, Gildea and Smirnow.⁶

This method is still subject to improvement, particularly with regard to the preliminary precipitation, ashing and other manipulation of the plasma. Nevertheless, the data obtained in this laboratory on the final determination (Table 1) illustrate its dependability and usefulness. In other words,

TABLE 1. *Determination of Plasma Hormonal Iodine.*

FUNCTIONAL RANGE	EQUIVALENT PLASMA CONCENTRATION (P) microgm./100 cc.	TIME FOR REACTION (T) min.	CONSTANT (P X T)
Myxedema	1	17 22	20
	2	9 10 10	20
	3	6 7	20
	4	4.6 5.2	20
	5	4.3	22
	6	3.5	22
	7	2.6	18
	8	2.5	20
Normal	10	2.2	22
	12	1.7	20
	14	1.4	20

under standard conditions, the amount of iodine in the aliquot is inversely proportional to the time observed. The value of the constant, of course, depends on the temperature adopted for the procedure and other factors that must be controlled. It should be noted that the normal amount of iodine in 1 cc. of plasma is 0.00000005 gm.

This method, as it is improved, is undoubtedly destined to extensive clinical use. Plasma can even be mailed to laboratories, packaged like Wassermann samples, over considerable distances. Because a single determination of basal metabolic rate is notoriously unreliable, and because Salter, Bassett and Sappington⁷ found the plasma hormonal iodine to be a more reliable clinical diagnostic procedure than determination of the basal metabolic rate, this method will ultimately prove important.

Determination of 17-ketosteroids. Pincus's⁸ reaction is likewise in use in this laboratory, and is presenting advantages over the Zimmerman type of reaction,⁹ employing meta-dinitrobenzene. The latter reagent, unfortunately, reacts with urinary pigments or chromogens to yield false colors that confuse the final determination. Various attempts to correct for this large and variable blank have not proved satisfactory.¹⁰ The values in Table 2,

however, obtained by Dr Raymond Cahen in this laboratory, indicate that the Pincus reagent (an timony trichloride) may be incorporated in a simplified urinary ketosteroid technic that will facilitate widespread clinical studies of androgen excretion. The colors developed by this reagent are

TABLE 2 Determination of 17 Ketosteroids

AGE	SEX	CLINICAL DIAGNOSIS	EXCRETION OF 17 KETOSTEROIDS (mg/24 hr)					
			ZIMMERMAN			PINCUS		
			α	β	Total	α	β	Total
37								
44	F	Addison's disease (critical)	3.7	0.7	4.0	2.2	0.7	3.1
40	F	Addison's disease (controlled)	7.3	2.2	9.2	3.7	0.9	4.8
26	F	Virilism	20.5	2.2	22.7	18.2	2.7	20.5
26	F	Virilism	24.8	9.3	31.0	14.8	2.4	16.6
21	F	Normal	7.4	0.7	8.3	5.9	0.7	6.0
5	F	Normal	2.2	1.1	3.6	1.0	0.5	2.2

in the blue-green and yellow-green range, instead of the yellow-red range of the Zimmerman reaction.

It will also be observed that the general range of values given by this reagent is lower than that of the Zimmerman reaction. Furthermore, there are qualitative differences between the two reactions in that they do not measure the same ketosteroid configurations. Some of these qualitative differences may be summarized. After heating with antimony trichloride and dilution with glacial acetic acid, an intense blue color (absorption maximum at 610 m μ) is developed by androstenedione and its isomers and by androstenedione-17. Dehydroandrostenedione and pregnandiol show weak, yellow blue colors. The shade of color varies with the diluent. Thus, in chloroform, androstenedione shows absorption maxima at 560 and 620 m μ .

Quantitatively, the chief difference from the Zimmerman reaction shown by neutral extracts of urine occurs in the nonalcoholic ketonic fractions. As shown by Table 2, there are also considerable differences in the beta-ketosteroid moiety. In general, however, these discrepancies do not obscure the interpretation of the results in terms of the present concepts of ketosteroid metabolism.

In a previous article¹¹ discussed clinical vitamin determinations and pointed out that biologic methods were subject to several sources of error. Since that time, however, intensive work has been done in this field, especially with regard to the vitamin B complex. The field is too large to be reviewed in this article, and I shall therefore mention only the fermentometer method developed by Schultz, Atkin and Frey.¹² This procedure is based on the finding¹³ that the rate at which certain yeasts ferment glucose may be increased by

the addition of thiamine chloride. Although the original article describes apparatus of gross size, the procedure can readily be adapted to the microrespirometer (Warburg) technic.

Previously, considerable inaccuracy was introduced by the presence in biologic materials of a substance or substances that, like thiamine, also speed up fermentation. This substance, called "PAYF" (pyrimidine accelerating yeast fermentation),¹⁴ may be closely related to or identical with 2-methyl-5-ethoxymethyl-6-aminopyrimidine. At any rate, Schultz, Atkin and Frey¹⁵ have largely eliminated this error by subjecting a second aliquot to the action of sodium sulfite, which destroys the thiamine. Thus the first sample gives thiamine plus PAYF and the second PAYF alone, which may be as large as 40 per cent of the total. By this difference between the samples, the thiamine is determined. The surprising accuracy of the procedure is illustrated by the series of assays in Table 3, performed in this laboratory by Dr. Rigby Roskelley. It must be confessed that this particular series is more consistently accurate than many routine series, but it can be duplicated readily if special care is taken.

Although precautions must be taken to control the sample of yeast used, and to check each type of biologic material by known additions of thia-

TABLE 3 Assays of Known Solutions of Thiamine by Fermentation Technic

KNOWN THIAMINE CONTENT	ASSAYED THIAMINE CONTENT
microgram	microgram
1	0.97
	1.01
	0.99
	0.99
	0.99
	1.07
2	1.93
	1.99
	2.00
	2.00
	2.00
	2.00

mine examined simultaneously with the unknown, the method is far less irksome than the best chemical methods now available. Furthermore, for most purposes it is quite as accurate.

Suitable methods for other vitamins are now being worked out on the same principle, but they have not yet been so extensively tried as the thiamine procedure.

HYDROGEN-ION CONCENTRATION

For years physicians and medical students have struggled with the distinction between hydrogen-ion activity (measured as pH) and alkali reserve

They have learned that a diminution in plasma bicarbonate often indicates acidosis—but not always. This traditional use of carbon dioxide as an index of hydrogen-ion activity in large part grew out of the technical fact that, formerly, direct measurement of plasma pH was extremely difficult. As a by-product of this indirect physicochemical approach to the measurement of hydrogen-ion activity, by means of the Henderson-Hasselbalch equation, a great deal of obscure thinking has flourished in clinics.

In a sense, this Gordian knot has been severed by the development of convenient methods for direct measurement of the acidity of the blood. The actual procedure requires only a few minutes, and only 1 or 2 cc. of blood. No great precaution is necessary against loss of carbon dioxide, beyond collecting the blood under mineral oil. A delay of even two or three hours is permissible before reading. The blood is treated with a suitable oxalate-fluoride mixture to prevent clotting and glycolysis.

The chief disadvantage of the method, which employs glass electrodes, is that the thermoionic amplifying devices required for the apparatus are expensive. They are, however, permanent, and in many laboratories much of the potentiometric equipment is already available.

Several types of apparatus have been described. One of the best procedures, however, is that of Nims.¹⁶ This method has the advantage that it measures the blood pH in terms of its deviation from that of a known buffer. In this way uncontrollable variations in the apparatus or environment are largely compensated.

If one wishes to construct the apparatus from general equipment, one of the better circuits is described by Nims. In addition to a good potentiometer, a thermoionic amplifier is necessary to activate a recording galvanometer, which is used as a nul-point instrument. Several excellent commercial instruments, however, are available in effectively compact form.

In making the determination, which requires only a few minutes, it is important that the blood and glass electrode be maintained at body temperature. This is essential because one is looking for rather small shifts in the activity of hydrogen ions and the temperature coefficient of the thermodynamic equilibrium involved is rather large. The electrode itself should be housed in a special water jacket, through which a stream of water circulates from a thermostatically controlled bath. It is convenient, also, to warm the tuberculin syringe from which the blood is delivered to the electrode. With special care, as little as 0.2 cc.

of blood may suffice for the final determination, but 1 to 2 cc. of whole blood is ordinarily used.

Formerly, extreme precautions were taken with fresh blood to prevent loss of carbon dioxide, and the glycolysis of glucose was neglected. It now appears that the formation of lactic acid from the blood sugar is the more important source of error. Accordingly, fluoride or some similar toxic agent is required.

The profound effect of changes in the hydrogen-ion concentration on rates of biologic reactions is so well known that it needs no further comment. Although its importance has been appreciated in clinics, the technical difficulties of measurement have caused greater emphasis to be placed on electrolyte patterns, which often have been misleading because they were incompletely determined. In any large clinic with an active laboratory service, there should no longer be any difficulty in deciding whether acidosis or alkalosis exists. If, however, one or the other abnormality in hydrogen-ion activity is found, it may still be desirable to determine the alkali reserve as a gauge of the severity of the disease and as an aid to therapy or prognosis. In my opinion, however, the problem of laboratory "diagnosis" can now be solved satisfactorily in a few minutes in any well-equipped clinic. Furthermore, the severity of the acidosis or alkalosis can be expressed quantitatively in terms of shift of pH.

ENZYMES

In a previous article I¹⁷ referred to the clinical applications of the measurements of blood enzymes, for example acid phosphatase, alkaline phosphatase and amylase. To this list must now be added carbonic anhydrase. Physiologists interested in the rate of carbon dioxide transfer from blood to alveolar air have made many fundamental studies of this biologic catalyst. Among the most informative are those of Roughton and his associates.^{18, 19}

Recently at New Haven, Stevenson²⁰ has made an important clinical application in the study of the newborn. He finds that the concentration of circulating carbonic anhydrase is low in the newborn, and even lower in the premature infant. It is likely to be especially low in such infants as are cyanotic without obvious reason. The mortality rate in these cases is high, but post-mortem examination reveals little cause for death. Certainly, the older notion of congenital atelectasis—that is, failure of the fetal lung to expand at the first gasp—is fallacious in these cases. When, however, such infants are transfused, their blood enzyme becomes elevated rapidly and their cyanosis disappears. Furthermore, the mortality rate is considerably lowered. This striking clinical result

is a fascinating outcome of an abstruse study of chemical kinetics.

The enzyme concerned has been prepared in crystalline form by Scott and Fisher.²¹ Its action is to expedite the liberation of carbon dioxide from carbonic acid. Without its influence this gas cannot be unloaded from the blood at a speed commensurate with the rate of the pulmonary circulation. It is interesting that this delay indirectly impedes the uptake of oxygen, for which reason oxygen therapy is of no avail in the infants studied by Stevenson.

SUMMARY

A new field of clinical chemistry is arising that deals with biologic catalysts. The study of these substances involves specialized microtechniques, which are themselves often catalytic. Such measurements afford highly specific information concerning the functional effectiveness of definitive physiologic mechanisms. They also give momentary estimations of the dynamic rate at which such systems are operating.

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Annual Meeting, May 24, 1943

THE annual meeting of the Council of the Massachusetts Medical Society was called to order at 7.00 p.m. in the Georgian Room of the Hotel Statler, Boston, on Monday, May 24, 1943, by the president, Dr. George Leonard Schadt, Hampden; 204 councilors were present (Appendix No. 1).

The Secretary presented the record of the stated meeting held February 3, 1943, as published in the *New England Journal of Medicine*, issue of March 18, 1943, and moved its approval. This motion was seconded and it was so ordered by vote of the Council.

Dr. Schadt, at this point, called the death of Dr. Charles S. Butler, treasurer of the Society, to the attention of the Council. He said his death took place on February 23, 1943, after a long illness and that the Massachusetts Medical Society had lost a great friend in his passing. He added that Dr. Butler had a gentle, sweet, kind character, that he was a gentleman of the old school

whose life exemplified what was in the poet's mind:

From first beginnings out to undiscovered ends,
There's nothing worth the toil of winning but laughter
and the love of friends.

He spoke of Dr. Butler's great devotion to duty, oftentimes at the expense of his health. At the request of the President, the Council stood in silence for two minutes in tribute to the memory of Dr. Butler.

Dr. Reginald Fitz, Suffolk, moved that the President appoint a committee to draw up suitable resolutions on the death of Dr. Butler. This motion was seconded by Dr. Walter G. Phippen, Essex South, and it was so ordered by vote of the Council.

Dr. Schadt appointed to the committee Dr. William H. Robey, Dr. David Cheever and Dr. Reginald Fitz.

Dr. Harold R. Kurth, Essex North, was recognized. He read a statement (Appendix No. 2)

which had already been published in the proceedings of the February 3, 1943, meeting. This matter was presented at this time as the result of a directive issued by the Council on February 3, 1943. It concerned a difference of opinion as to an individual's acceptability for membership in the Massachusetts Medical Society—the local committee on membership favoring the candidate and the state committee opposed. Dr. Kurth offered the following motion:

It is the sense of the meeting that the essential responsibility of whether or not graduates of unrecognized or foreign schools shall be admitted to the Society lies in the local membership committees, and that the central committee should concern itself essentially with the responsibility of seeing that no undue pressure has been brought to bear upon the local boards, either to endorse, or to bar, the approval of candidates.

This motion was seconded by Dr. Elmer S. Bagnall, Essex North, who said that he was one of three who examined the candidate in question. He added that in all the years he had been a member of the board of censors he had never seen a more adequate consideration to an applicant for admission to the Society than in this case. He disclaimed any intention of upsetting the by-laws. He said the motion had for its purpose an expression of opinion from the Council that the local committees have better opportunity to know those possessed of qualifications for membership in the Society.

Dr. Roy V. Baketel, Essex North, was recognized. He spoke as follows:

I have been a censor for quite a period of years. I should hate to tell you just how long. It has been longer perhaps than my memory; and I might say that at our meeting earlier in the month the officers in the district saw fit to give me five years more, so perhaps they do believe that I have tried to treat the applicant for membership in the Society in a reasonably honest, fairminded, square way.

Now I should like to say, in addition to the facts that have already been presented, because to me this is a rather strong fact in our failure to understand the decision handed down by the central committee, that we had, in November, two candidates, both graduates of a Grade C school, both men of foreign extraction, both practicing in Lawrence, both with the same type of recommendation. These recommendations came from men in long practice in Lawrence and its vicinity—men who had had contact with these applicants, men whose advice we believed in, men whose purpose we believed was honest.

The first of these applicants came from a below-standard school. He passed our examination very satisfactorily, and these recommendations, which were practically unanimous, were accepted by the central committee, and the man is today a member of the Massachusetts Medical Society. So far as we knew at

the time there was practically no difference—indeed, I am willing to state it a little more strongly—there was no difference in the qualifications of these men in our minds. Because of the fact that they came from subpar schools they were interrogated at the time more closely than might have been the case had they come from Grade A schools. And, further than that, we went into the factor of citizenship to a considerable extent. I know that we are all anxious in the light of the war to be sure that every man who is a member of this society, or a member of any American organization, is a patriotic citizen. We stood fast on those lines as to both of these men. The examination also included very specifically the ethics practiced by these men. We tried to obtain from them their belief in ethics, their attitude toward ethics, their attitude toward their fellowman in the daily pursuit of their practice, their attitude toward the patient under varying conditions; in fact, we tried to delve and did delve more deeply into their consciences than we have done with the average man from the average school.

We were certainly amazed when the report came back that one man was accepted and the other man was rejected. We believe that an injustice has been done. Certain correspondence took place between our secretary and the chairman of the general committee asking what the charge was, what we had left unsaid or undone, if they had information we did not have, and if they knew anything about this man that was against him in any way? We had no answer to that inquiry. We believed that they had no more information than we had, and I think they admitted it; therefore, it was all the harder for us to understand why one man should be accepted and the other man rejected.

As has been stated, we have no fault to find with the provisions of the by-laws. We think they are ample. We think their interpretation needs to be a little broader. We think they should be constructive; and we think, too, that in construing them considerations of a humanizing nature should apply when we pass upon applications of those whose circumstances may not be as fortunate as ours. We tried to assume such an attitude at that meeting, and not only did we want to be human to them but we wanted to be fair and square in every way. We still think these by-laws should not be changed but that interpretation of them should be along a broader basis and on more humanitarian lines.

Dr. George D. Henderson, Hampden, said that one might get the idea from the discussion that Dr. John P. Monks did not back up the central committee. This was a wrong impression. He expressed it as his own thought that all these candidates should be approved by the central committee. He added that he was opposed to the motion.

Dr. Fred H. Allen, Hampden, expressed a desire to know more of the facts before being called upon to vote on the question. He asked that some member of the central committee be asked to state that committee's point of view in this matter.

Dr. Harlan F. Newton, Suffolk, chairman of the Committee on Membership, responded. He said

that there was no question that the proper agent to examine candidates from substandard schools is the local committee. The approval of such committees, however, is often sent to the Committee on Membership without being accompanied with the reasons for such approval, and at times the Committee on Membership gets the feeling that the local committee, while it does approve the candidate, is not particularly keen about him. The question, he added, is simply this, Does the Council wish the local committees to have the entire say as to whether the candidate shall be passed along to the censors or does it want an intermediate check by the Committee on Membership, as at present provided for in the by laws?" Dr Newton pointed out that three supervising censors sit with the Committee on Membership and that, in spite of all this, mistakes may happen and may have happened in this particular case.

Dr Kurth disclaimed animus against the central committee. He added that local committees are in a favored position to probe the background and the ethics of candidates from substandard schools. Because of this it is difficult to understand why the central committee disapproves of a candidate already approved by a local committee.

Dr Arthur M. Jackson, Middlesex South, expressed the thought that the Council was wasting its time by voting something which attempted to upset the by laws.

Dr Curtis C. Tripp, Bristol South, moved that the whole matter be laid on the table. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

REPORT OF EXECUTIVE COMMITTEE

The Secretary, in presenting the report (Appendix No 3), said the Executive Committee had now been in existence for two years. He added the circumstance which created this committee was indeed fortuitous inasmuch as it has enabled the Society to act promptly in matters pertaining to the war.

The committee, on the recommendation of the Committee on Membership, under the provisions of Chapter I, Section 5, of the by-laws, retired sixteen fellows, under the provisions of Chapter I, Section 7, allowed twelve fellows to resign, under the provisions of Chapter III, Section 3, allowed three fellows to change their membership from one district to another without changing their legal residence; under the provisions of Chapter I, Section 10, readmitted four fellows who had resigned while in good standing, readmitted two fellows who had been deprived of membership for nonpayment of dues, provided they discharged all

their obligations to the Society within one month; under the provisions of Chapter I, Section 6, remitted the dues, including those of 1943, of ten fellows, and under the provisions of Chapter I, Section 8, deprived fourteen fellows of membership for the nonpayment of dues.

The committee in conference with the Committee on Membership, under a directive of the Council given on February 3, 1943, recommended the following:

Fellows of the Massachusetts Medical Society shall not be required to pay further dues during their period of active service in the United States Army, Navy or Public Health Service. Those so requesting may receive the *New England Journal of Medicine* upon request and payment of the \$4.00 subscription fee.

The above does not apply to fellows going into active military service during the first year of fellowship in the Society.

The Secretary moved the adoption of the recommendation. This motion was seconded by a councilor.

Dr F. H. Allen asked why the Marines were left out. It was explained that the Marines had no distinct medical service, such being supplied by the Navy.

Dr Fitz, calling attention to the fact that there may be a few members of the Massachusetts Medical Society serving with the medical branch of the Canadian Army, offered an amendment to the recommendation so as to include the latter. This amendment was seconded by a councilor. The maker of the motion and its seconder having accepted the amendment, the chair declared it a part of the original motion. The recommendation was adopted by vote of the Council.

The committee reviewed the report of the Committee on Membership with regard to the establishment of a junior membership and approved of its recommendations.

The Council on February 3, 1943, referred to the Executive Committee four recommendations offered by the Auditing Committee of 1943. These recommendations are as follows:

That the investment of the Society's funds should be under the direction of a professional investment company.

That the report of the accountant should be more complete and include a list of investment transactions.

That the latter should include a statement that the report of the fiscal year is reconciled with the report of the preceding year.

That the duties of the Auditing Committee be turned over to a businessman trained as a bank examiner.

The Secretary said in connection with the first recommendation that the committee received from

the investment firm of Loomis-Sayles and Company an analysis of the Society's investment portfolio and certain advice with regard to a safe and profitable way in which this portfolio might be handled in the future. It was observed that there were too many items in the list, that the total yield was only 2.82 per cent and that the latter might be very materially increased without jeopardizing the principal. This firm would charge for handling the Society's investments 0.5 per cent on the first \$300,000 and 0.4 per cent on additional capital.

The Secretary read a letter addressed to Dr. Eliot Hubbard, Jr., by the New England Trust Company in which this bank explained its method of operation under four headings as follows:

To appraise and review quarterly the list of securities making up the account and to submit in writing the quarterly appraisals with recommendations for changes in investments that seem to be desirable.

To recommend changes of investments between quarterly reviews if desirable.

To confer with the treasurer at any time regarding the Society's investment problems.

To receive as compensation annually 0.2 per cent of the market value of the property in the account at the date of the original appraisal for the first year, and at the date of the anniversary appraisals for subsequent years.

The cost to the Society for handling the portfolio in this manner would be approximately \$420 per year.

The Secretary reported that the committee recommended the employment of investment counsel. He moved the adoption of this recommendation. This motion was seconded by a councilor.

The Secretary explained that the authority for the investment of the Society's funds rests, under the by-laws, in the hands of the Treasurer and that the Council at this time should do no more than say to the Treasurer, "We approve of you having at your disposal investment counsel—either that supplied by banks or that furnished by investment-counsel firms." The recommendation was adopted by vote of the Council.

With regard to the second recommendation of the Auditing Committee of 1943, the committee took notice of the fact that auditing committees are already provided with full authority, under the by-laws, to insist on the matters set forth in this recommendation and that, furthermore, it is the opinion of the committee that auditing committees should so insist.

The Secretary moved that the Council concur in these opinions. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

The committee reported that it concurred in

the feeling of the Auditing Committee that the interval between the closure of the Treasurer's books and the stated meeting in February is too short to enable such a committee to do the kind of job which should be done. The Secretary announced that under new business amendments to the by-laws would be offered whereby the Treasurer's report and that of the Auditing Committee would be presented to the Council at the annual meeting instead of at the stated meeting in February.

The committee considered the recommendation made by the Committee to Aid the Boston Medical Library. This recommendation would have the Massachusetts Medical Society turn over to the Boston Medical Library the earnings of the Society's building fund. The committee expressed the opinion that a vote of the Council passed in June, 1929, makes this impossible. In connection with this subject, the committee offered two recommendations:

That the Massachusetts Medical Society acquire the space now occupied by the *Journal of Bone and Joint Surgery*.

That the Massachusetts Medical Society pay to the Boston Medical Library as rent a sum of money, up to \$6500 per annum, for its quarters thus enlarged.

The Secretary moved the adoption of the first recommendation. This motion was seconded by a councilor, and it was so ordered by vote of the Council. The Secretary moved the adoption of the second recommendation, and the motion was seconded. There was some discussion as to whether or not the word rent in the recommendation might involve the library in certain troubles anent its tax-free status. Dr. Edwin R. Leib, Worcester, asked if the legal side of the matter had been looked into. The Secretary replied that it had. Dr. David Cheever, Suffolk, confirmed this and said that it had been learned authoritatively that rent paid to a philanthropic, charitable or educational institution and used by that institution, for the purpose for which it exists under its charter, does not constitute rent in the sense of being taxable income. The recommendation was adopted by vote of the Council.

The committee reported that it had reviewed and approved the report of the Committee on Medical Defense and that of the Committee on Expert Testimony. The committee commended the report of the Committee on Public Relations to the attention of the Council.

The committee reported that the Army had approved of a plan to subscribe to the *New England Journal of Medicine*, placing a copy in every Army hospital of twenty-five beds or over. It

defeated a motion to send one hundred copies of the *Journal* to the Navy free.

The committee recommended that stated meetings of the Council begin at 10:00 a.m. and, while there is any business to transact, do not adjourn for lunch until 2:00 p.m. The Secretary moved the adoption of this recommendation. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

The committee acknowledged the receipt of a communication from Dr. Charles F. Wilinsky et al., of the staff of the Beth Israel Hospital, including a protocol governing a plan for the care of the practices of such members of its staff as have entered or will enter the armed forces. The committee recommended that this matter be referred to the War Participation Committee and that this committee report to the Executive Committee at its next meeting. The Secretary moved the adoption of this recommendation. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

The committee recommended that the Committee on Arrangements be instructed to provide for an exhibit and a luncheon meeting on anesthesia and for the suitable advertising of this meeting and exhibit in the program of the annual meeting. The Secretary moved the adoption of this recommendation. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

The committee acknowledged the receipt of a letter from the National Conference on Medical Service, including a resolution which it was intended to offer at the meeting of the House of Delegates of the American Medical Association on June 7, 1943. This resolution called for the creation of a new committee of the American Medical Association made up of certain officers of that organization and so forth. This committee would maintain a Washington office and be supported by an appropriation from the American Medical Association of not less than fifty cents and not more than one dollar for every member of that organization. The committee recommended that this matter be referred to the Massachusetts delegation to the House of Delegates of the American Medical Association without prejudice. The Secretary moved the adoption of the recommendation. This motion was seconded by a councilor, and it was so ordered by a vote of the Council.

The committee reviewed a list of appointments made by the president-elect, Dr. Roger I. Lee, and approved of the same.

The Secretary moved the adoption of the Executive Committee's report as a whole. This mo-

tion was seconded by a councilor, and it was so ordered by vote of the Council.

REPORT OF COMMITTEES

Committee on Arrangements—Dr. Gordon M. Morrison, Middlesex South, chairman.

Dr. Morrison reported as follows:

We have no formal report to render. The annual meeting is our report. After having served on this committee one year I found myself precipitated into the chairmanship. Drs. Faxon, Halsted and Sturgis are all in the armed forces. During this last year Dr. Schadt, our president, Dr. Lee, our president-elect, and Dr. Tighe came to our meetings faithfully and helped us out a great deal. The committee that I have been fortunate enough to have work with me this year—Roy Heffernan, Richard I. Smith, Sidney Wiggin and Guy Bailey—could not have been a better committee for any chairman to have work with him. There is just one more person that I want to mention as having been indispensable to our committee last year, and that is our executive secretary, Mr. Robert Boyd. He has done an excellent job.

Dr. Morrison moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Publications—Dr. Richard M. Smith, Suffolk, chairman.

No report.

Committee on Membership—Dr. Harlan F. Newton, Suffolk, chairman.

Dr. Newton reported (Appendix No. 4) that his committee, while favoring in principle the establishment of a junior membership in the Massachusetts Medical Society, did not believe that this was the time to do it. He moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Finance—Dr. John Homans, Suffolk, chairman.

No report.

Committee on Ethics and Discipline—Dr. Ralph R. Stratton, Middlesex East, chairman.

The chairman reported as follows:

Your committee has held four meetings during the past year—at which thirty-four cases were discussed. These cases varied from requests for advice as to ethical procedure to complaints of member against member charging violation of the code. Several of these cases, which were involved in court procedures or might be so involved, were laid on the table pending legal action. All other cases were thoroughly investigated and decisions reached based on the data obtained. The most serious one—a charge of violation of Act III, Section 8, of the Code

of *Ethics* of the American Medical Association — was happily settled by an apology being rendered by the defendant to the injured fellow.

It is an interesting thought that throughout the year not one member has been asked to resign, or his name sent to the President for admonishment. All cases have been settled in committee and the decisions accepted by the fellows concerned.

At present there are before the committee two complaints of exorbitant charges against fellows, one case of improper advertising and three serious complaints of violation of the *Code of Ethics*. These are being thoroughly investigated and will be reported at a future meeting.

I cannot close this report without expressing the appreciation of his fellow committee members to Dr. William Brickley for his very kind gift of recent date, the pleasure of which we have sampled already.

Committee on Medical Education — Dr. Robert T. Monroe, Norfolk, chairman.

No report.

Committee on Public Health and Subcommittee on Public Education — Dr. Francis P. Denny, Norfolk, chairman.

In the absence of Dr. Denny, the Secretary read the report, which is as follows:

The series of broadcasts carried on by these committees with the title "Green Lights to Health" were discontinued in March, 1942.

This spring, at the instigation of the Massachusetts Department of Public Health, and with the offer of a favorable hour by Station WEEI, 4:30 to 4:45 p.m. on Wednesdays, the committee decided to arrange for a series of ten broadcasts. This series has been given the title "Health on the Home Front," and was started on April 7 and will end on June 9.

We are very grateful to the members of the Society who consented to give these broadcasts despite the many demands on their time.

The Secretary moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Medical Defense — Dr. Arthur W. Allen, Suffolk, chairman.

Dr. Edward D. Gardner, Bristol South, offered report, which is as follows:

At present, there are seven cases pending. During the past year, two cases have been disposed of — one, for lack of prosecution; the other, with a companion case, was nonsuited when it was reached for trial.

There have been two new cases entered during the past twelve months.

We wish to call attention again to the possibility of malpractice suits against fellows while in military service. We also urge that all men re-establish their insurance protection at the earliest possible moment and return to practice in case they have dropped their protection while on military duty.

Dr. Gardner moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Society Headquarters — Dr. William H. Robey, Suffolk, chairman.

No report.

Committee on Industrial Health — Dr. Dwight O'Hara, Middlesex South, chairman.

In the absence of Dr. O'Hara, the Secretary read the report, which is as follows:

At the last meeting of the Council the Committee on Industrial Health announced that it would hold another all-day meeting similar to that held at the Harvard Club last November. This was done, with an entirely new program, on April 24, 1943. One hundred and sixty registered, most of whom were present for the luncheon at noon, which was addressed by Dr. Alice Hamilton, and at which we were also honored by the presence of Dr. Robert H. Parry, health officer of Bristol, England, and by the presence of President Schadt.

The committee has continued to keep in touch with the State Department of Labor and Industries and with the State Department of Public Health, and has made a few fresh contacts with representatives of the Associated Industries of Massachusetts. The committee has advised several employers concerning medical services and has been able to aid in the placing of a few physicians in industrial medical work. It has met with a representative of the Council on Industrial Health of the American Medical Association, has prepared papers for publication in both medical and industrial journals, has delivered a broadcast on industrial health in co-operation with the Committee on Public Health, and has endeavored to be as active as possible on all fronts during this period of unprecedented industrial output.

The Secretary moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Massachusetts Committee on Procurement and Assignment — Dr. Reginald Fitz, Suffolk, chairman.

This report (Appendix No. 5) contained the following resolution:

WHEREAS, The War Manpower Commission has announced that there is immediate need for more physicians to serve as medical officers in the armed forces of the United States; and

WHEREAS, The War Manpower Commission has announced that Massachusetts should supply more medical officers than have so far been commissioned from the state; and

WHEREAS, A plan has been suggested by the War Manpower Commission through which the enrollment of medical officers may be accelerated with the help of county or district medical societies in certain states; therefore, be it

RESOLVED, That reviewing committees be established by each district society, the members of which shall be nominated by the district-society presidents and appointed by the president of the Massachusetts Medical Society. Such committees shall serve for the general purposes outlined in this report.

Dr. Fitz moved the adoption of the resolution. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Dr. Fitz moved the acceptance of the report as a whole. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Public Relations—Dr. Elmer S. Bagnall, Essex North, secretary.

Dr. Bagnall reported as follows:

The committee has conferred with the president of the Massachusetts Nurses Association and made some progress toward meeting and understanding mutual problems.

The Ellison subcommittee on relations with the Industrial Accident Board has made progress and has reason to believe the proposals made by us are being favorably considered by the board and the insurance carriers.

In this emergency we accept the obligation to initiate remedies to correct, so far as practicable, manifest deficiencies in the distribution of medical care by enlisting co-operation of all agencies concerned. Each district public relations committee should invite more intelligent co-operation of the public by whatever form of ethical propaganda best suits local needs. The doctor should exercise judgments based on the whole public interest when considering the request by his patient for hospital occupancy or for full-time special nursing. Serious nursing shortages exist in many communities. The district public-relations committee should stimulate formation of district nursing councils as outlined in a well-prepared prospectus concerning organization methods and component representation, which is procurable from Massachusetts State Nursing Association, 420 Boylston Street, Boston. Local telephone exchanges need better understanding of the problems involved in so-called versus real emergencies. We might attempt a practical definition of what is and what is not an emergency. Each district public-relations committee should move toward improvements in this field. The district public-relations committee should exert all reasonable efforts to prevent default of doctors in response to real emergencies even though our physical resources have been strained by the demands made upon them.

Dr. Bagnall moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Subcommittee on Tax-Supported Medical Care—Dr. Bagnall, chairman.

Dr. Bagnall reported as follows:

Because your chairman is able in his capacity as chairman of the Medical Advisory Board of the Department of Public Welfare to handle such problems

as are now arising in this field no meetings of the committee have been needed.

Policies had been agreed upon last year by the department and the Society. The department is endeavoring to extend these policies to local administration of the welfare medical care.

Dr. Bagnall moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Subcommittee Concerned with Postpayment Medical-Care Costs through Banks—Dr. Bagnall, chairman.

Dr. Bagnall reported as follows:

The Massachusetts Bankers Association has a committee co-operating with our committee to get a plan in operation in October. It is to supply the applications, note forms and so forth. The Massachusetts Medical Society is to endeavor to inform its members regarding the purpose and machinery of the plan. Suitable propaganda can be made available to the doctor by the Society for informing the patient about this means of budgeting for payment of the costs of medical care. All banks dealing with consumer credit will co-operate by taking up the notes and paying the doctor directly if the patient's credit justifies.

There are about 4600 active fellows in the society and it would cost about \$550.00 to inform the doctors and to provide them with machinery to utilize its facilities.

The Council, at the last annual meeting, authorized the institution of this project. We recommend that the president be authorized to add to the committee enough additional members to introduce the plan properly when the appropriation is approved by the Committee on Finance.

By way of additional information Dr. Bagnall pointed out that one year ago the Council adopted the principle of postpayment medical care as suggested by the National Shawmut Bank and authorized the Committee on Public Relations to proceed to put the plan into operation. Dr. Bagnall explained that this matter was not referred to the Committee on Public Relations or to the Executive Committee because of lack of time.

He moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee to Meet With the Medical Advisory Committee of the Industrial Accident Board—Dr. Daniel J. Ellison, Middlesex North, chairman.

No report.

Subcommittee on Prepayment Medical-Care Costs Insurance—Dr. James C. McCann, Worcester, chairman.

The report (Appendix No. 6) was presented by Dr. McCann.

Dr. Fitz moved its acceptance. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Legislation—Dr. Brainard F. Conley, Middlesex South, chairman.

This report, which was offered by the chairman, is as follows:

When the Great and General Court began its session for the year 1943, His Excellency, Governor Saltonstall, made the request, that because of the war, the Legislature complete its work within as short a time as possible. As a result of this request there appeared on the front page of every weekly issue of the Bulletin of Committee Work of the General Court, the following paragraph, to quote:

Because of the present wartime necessity to expedite legislative business, the time allowed for arguments may be limited at all committee hearings. It is therefore urged that all arguments be concisely stated, and that detailed or supplementary facts be submitted in writing. All information submitted will receive careful consideration. The co-operation of all interested parties in furthering this method will be most helpful.

Your committee wishes to report strict compliance in every respect with this pattern of procedure.

We also wish to report that this committee is very appreciative of the courteous and intelligent co-operation extended by the members of the joint Committee on Public Health of the Legislature.

The *New England Journal of Medicine* of May 13, 1943, contains a bulletin of as much committee work as had been acted upon up to the latest date possible of printing before this meeting of the Council. As soon as the present session of the Legislature closes, which will in all probability be within the next two weeks, all the bills of interest to the Society will have been acted upon and a completed list will be published in a similar manner.

In the report of this committee to the Council in the February meeting we acknowledged our cognizance of the anticipated decrease of income to the Society for this year. We have continued our careful watching of expenses and have endeavored to keep them down, in spite of the fact that the amount of work done was, little, if any, less than in previous years. We hereby submit for your information the following financial savings.

In order to reveal the amount of money saved, we must first of all call to your attention that the legislative committee spent, in round numbers, \$3900 during the last biennial session. Of this amount \$1500 was spent for legal counsel. This year this committee made an arrangement whereby we could get what we considered the best possible legal advice and pay for only what we needed. Therefore, we found that we needed only \$50 worth of legal advice. This advice has been received and paid for, and we have saved \$1450. That same year the amount of \$218 was paid to the Legislative Reporting Service. To date, and the session is about over, we have received all the help we needed from that source and at a cost of approximately \$70. Here is a saving of \$148. Copies of the *Who's Who in the Legislature* cost us \$45, just the same as two years ago. Travel expense, telephone, telegraph, clerical hire and incidental expenses

have amounted to slightly over \$50. In other words, this year your committee on legislation will have completed its work with a minimum of expense, namely, about \$220, as against \$3850 two years ago—a saving of \$3630.

Dr. Conley moved the acceptance of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee to Examine WPA Records—Dr. Guy L. Richardson, Essex North, chairman.

Dr. Richardson reported as follows:

Work Projects Administration is at an end in Massachusetts. Since our last report to the Council we have not been called upon to adjust any differences between physicians and the WPA office.

The President of the United States has said that the WPA is entitled to an honorable discharge. Your committee requests its discharge, fearful it may be said of us as was said editorially of WPA itself. I quote: "We would go a little farther than the President. We would say, not only that the WPA is entitled to an honorable discharge, we would say it has been entitled to one for a long time."

Dr. Richardson moved the acceptance of the report and the discontinuance of the committee. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Cancer—Dr. Ernest L. Hunt, Worcester, chairman.

This report (Appendix No. 7) was offered by Dr. Hunt. It spoke of a meeting of the committee at which Mr. H. D. Fish, assistant managing director of the American Society for the Control of Cancer, Incorporated, presented a plan for popular education, in co-operation with the state program, which latter program has been backed by the experience and facilities of the Society. The committee thought that this plan was not expedient at this time. Dr. Herbert L. Lombard was present at this meeting and spoke of a two-day symposium on cancer that had taken place. This conference was held because it was realized that some type of cancer education should go on during the war. Out of it came a booklet, known as *Cancer: The what, whither, how*.

This report spoke of the improvement in the cancer situation in Massachusetts during 1942 in light of the report by Dr. Simmons on state-aided cancer clinics. It emphasized the fact that there must be no letup in the cancer-control effort because of the hardships imposed by the war.

The report concluded with the following statement: "It is our conviction that there is no substitute for the well-educated, experienced, conscientious doctor."

Dr. Hunt moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Postgraduate Instruction—Dr. Fitz, chairman.

No report.

Military Postgraduate Committee—Dr. W. Richard Ohler, Norfolk, chairman.

This report (Appendix No. 8) spoke of eleven exercises that were held at Fort Banks, ten at Camp Edwards, one at the Portsmouth Navy Yard and ten at Westover Field.

The committee expressed the view that this work had been very much worth while and that the officials of the Army and Navy felt likewise.

The committee offered the following recommendations:

That the committee be continued and directed to enlarge its activities as far as practical.

That an invitation be extended to the other New England state medical societies to co-operate in this project and that all medical officers of the Army and Navy in New England be offered postgraduate instruction in some form.

Further, that the Massachusetts Medical Society underwrite the expense of this effort.

Dr. Ohler moved the acceptance of the report and the adoption of the recommendations. This motion was seconded by a councilor.

Dr. Morrison asked how this postgraduate work fitted in with the postgraduate work of the federal government.

Dr. Ohler answered that he presumed that Dr. Morrison was referring to the plan announced in the *Journal of the American Medical Association*, issue of May 1, 1943. He added that this plan was under the auspices of the American Medical Association, the American College of Physicians and the American College of Surgeons and that it was still in the process of organization. He also said that in Boston, Philadelphia and Chicago such plans were already in operation and that it will be the policy of the committee controlling the plan, referred to by Dr. Morrison, to turn his work over to the groups which are already functioning.

The Secretary asked if he was correct in his understanding that the Military Postgraduate Committee was asking the Massachusetts Medical Society to underwrite the expenses incident to courses given in other states. Dr. Ohler answered in the affirmative, adding, however, that it was hoped that other societies in New England would ultimately share the expense. He said that the part of the Society, so far as it was related to other states, would be incidental only to getting the work started.

Dr. Carl Bearse, Norfolk, asked if it were not a bit dangerous to underwrite the project without knowing exactly how much money might be needed. Dr. Ohler expressed the thought that the \$500 would probably more than cover the expense.

Dr. Ohler amended his original report so as to add at the end of the third recommendation the words "in an amount not to exceed \$500." The seconder accepted this amendment. The motion as amended was adopted by vote of the Council.

Committee on Physical Therapy—Dr. Franklin P. Lowry, Middlesex South, chairman.

Dr. Lowry reported as follows:

This committee is primarily interested in research and education.

During the past year it can report nothing completed in research.

It has, however, sponsored a program of lectures in physical therapy for the medical personnel at Fort Devens.

Dr. Lowry moved the acceptance of the report. This motion was seconded, and it was so ordered by vote of the Council.

Committee on Expert Testimony—Dr. Frank R. Ober, Suffolk, chairman.

Dr. Ober reported as follows:

I thought that it was inadvisable to make a formal report, the reason being that there are fifty-three articles being published on forensic medicine under the editorship of Dr. Hubert W. Smith. Several of these articles have already appeared in the May number of the *Annals of Surgery*. A number are coming out in the *Yale Law Review*, the *Harvard Law Bulletin*, the *Rocky Mountain Bulletin* and the *Lippincott Clinics*. These are all being edited in book form. As soon as all the articles have been published in the magazines, they will be put in the hands of the members of the committee, and we shall then consider plans of procedure. It seemed very wise to wait until all this new material had been published before the committee commenced its study.

Dr. Ober moved the acceptance of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Automobile Insurance Claims—Dr. Henry C. Marble, Suffolk, chairman.

No report.

Committee on Convalescent Care—Dr. T. Duckett Jones, Norfolk, chairman.

No report.

Committee to Study the Practice of Medicine by Unregistered Persons—Dr. Richard Dutton, Middlesex East, chairman.

No report.

Committee to Meet with the Massachusetts Hospital Association — Dr. Walter G. Phippen, Essex South, chairman.

No report.

Committee on Maternal Welfare — Dr. Judson A. Smith, Suffolk, chairman.

No report.

Committee on Rehabilitation — Dr. William E. Browne, Suffolk, chairman.

No report.

Committee to Aid the Boston Medical Library — Dr. William H. Robey, Suffolk, chairman.

No report.

Committee on Ways and Means to Conserve Physicians' Energies — Dr. Bagnall, chairman.

No report.

War Participation Committee — Dr. William B. Breed, Suffolk, chairman.

No report.

Committee on Nominations — The committee was composed as follows:

W. D. Kinney, Barnstable; P. J. Sullivan, Berkshire; W. H. Allen, Bristol North; E. F. Cody, Bristol South; G. L. Richardson, Essex North; Bernard Appel, Essex South; R. R. Stratton, Middlesex East; W. H. Sherman, Middlesex North; Dwight O'Hara, Middlesex South; D. D. Scannell, Norfolk; D. B. Reardon, Norfolk South; W. H. Pulsifer, Plymouth; W. B. Breed, Suffolk; W. F. Lynch (alternate), Worcester; and B. P. Sweeney, Worcester North (there were no representatives from the Franklin, Hampden and Hampshire districts).

Dr. Walter H. Pulsifer, Plymouth, reported for the committee as follows:

President: Dr. Roger I. Lee, Boston

Vice-president: Dr. Daniel B. Reardon, Quincy

President-elect: Dr. Elmer S. Bagnall, Groveland

Secretary: Dr. Michael A. Tighe, Lowell

Treasurer: Dr. Eliot Hubbard, Jr., Cambridge

Assistant treasurer: Dr. Norman A. Welch, West Roxbury

Orator: Dr. Joseph C. Aub, Boston

The President asked if there were any nominations from the floor. There being none, he requested the Secretary to cast one ballot bearing the names and designations of the above. The Secretary announced that he had complied with this request, whereupon the President declared, amid great applause, the election of the officers for 1943-1944 as above listed.

APPOINTMENT OF COMMITTEES

Dr. Roger I. Lee, president-elect, in announcing the list of committees for 1943-1944, said that the

personnel of these committees was for the most part the same as that of 1942-1943. He moved that the list, which had already been approved by the Executive Committee, be likewise approved by the Council without being read. This motion was seconded by a councilor, and it was so ordered by vote of the Council. (The list will be published with the proceedings of the Society in the July 22 issue of the *Journal*.)

NEW BUSINESS

At this point in the meeting Dr. Peirce H. Leavitt, vice-president, assumed the chair and Dr. George Leonard Schadt was recognized. He spoke as follows:

The subject I am going to discuss with you is something that has been in my mind all year long, but it seemed to me that I should wait until the annual meeting of the Council before bringing it out. I shall present the plan I have in mind and shall ask Dr. Roger Lee, the incoming president, to exercise his prerogatives in appointing a committee.

The last war, as you know, was a comparatively short war. Many of us had been in practice five, ten or fifteen years when we went away. I happened to be in service for twenty-two months; some of us were in for ten, twelve or fourteen months—I believe the average was fourteen months. We got back into practice quickly. Some of us were lucky and had little trouble, but a lot of the men had difficulty getting started. I know because I talked with a great many of them. They needed a car, or they needed an office.

I can think of the story of one man, named Bill Smith, who came back and was quite a hero. He had been wounded severely and was brought home, and when he came back he met John Jones, a banker, who thought Bill Smith was a wonderful hero and told him what a fine fellow he was. And then he said to Bill Smith, "What can I do for you?" Bill replied, "I should like to see if I can borrow a little money." The banker said, "Of course you can. I'll be glad to give it to you. How much do you want?" "Twelve hundred dollars." "By the way, what about collateral?", John Jones asked. Bill Smith said, "This will be only for a year." However, the banker looked at him with a cold eye and said, "If you haven't any collateral I can't let you borrow the money." That was poor Bill Smith's position. He was a great hero, he had fought for his country in the war and he had been wounded, but he never got the \$1200—at least not from the banker.

A lot of men came back wounded and could not go into the type of practice they had engaged in before. They would have liked very much to have gone into something like refraction, but they did not have the money and they could not do it. As the result of the war many men lost out, not because of their service, but because of the fact that they could not afford to rehabilitate themselves.

I think we have a great opportunity in the Massachusetts Medical Society today. This war is different. It is a long war. It has already lasted, so far

as we are concerned, nearly a year and a half. It is going to last another two or three anyway. Our friends have gone, men who have been in practice five, ten or fifteen years. Many of those men are coming back wounded or in ill health. A surgeon may never be able to operate again. An internist may never be able to do that type of work. If he could do refraction or skin work, if he could get started with six or ten months' headway, it would be a great thing for him. A great many coming back are going to need special treatment until their wounds and their nerves are healed, and a majority of them are coming back without collateral.

My plan—and I have talked it over with a few men in the Society—is one to develop a fund in the Massachusetts Medical Society. Call it the Postwar Rehabilitation Fund. Let it run something on the order of the Morris Plan, any member of the Society being able, without embarrassment and without collateral, to make application for a loan. That application is endorsed by one or two members of the Society. The amount would be limited, and each application would receive careful consideration. Such a scheme could be easily put into effect. To come to us rather than to an otherwise affable banker or to a loan shark would save our friends and our colleagues a tremendous amount of embarrassment.

I can see that all this needs a lot of study, and all that I am asking of you tonight is to appoint a committee for that purpose.

I can visualize a man coming home and wanting to go to Harvard or Boston University or Tufts for post-graduate study. Incidentally, possibly the medical school should cut the fee in half or cut it out entirely for the ex-service man. The amount of the borrowing might be \$1000 or \$1500. That can be decided. The time in which the loan has to be paid might run one or two years. That, too, would be decided by a committee.

I can visualize further. I can see men who are not coming back, who are leaving wives, and children who need to be educated. There are quite a number of paths this plan might follow.

You say, "Well, where are you going to get the money?" I think the preliminary fund could be obtained by assessing every member of the Massachusetts Medical Society who had not had the privilege of serving with the armed forces, because of age, disability or another reason, \$10, with the opportunity of contributing more if he so desired. I think we could easily get \$50,000 to start with, and if we needed more we have a backlog of over \$200,000. Why does the Massachusetts Medical Society need \$200,000 in bonds? That is something which has been a source of worry to me all year long. We have done nothing with it. It has just been invested. There must be something constructive we can do with the money instead of having it lie in our treasury.

Dr. Schadt moved that the incoming President, Dr. Roger I. Lee, appoint a committee of fifteen to study the desirability and feasibility of such a plan and to submit reports of progress at the October and February meetings of the Council and a

final report at the annual meeting in May, 1944. This motion was seconded by Dr. William B. Breed, and it was so ordered by vote of the Council.

Dr. Leavitt read the following obituary:

Dr. Hanford Carvell, a member of the Council from the Essex South District, died on February 15, 1943, at the age of sixty-seven.

Born in Marysville, New Brunswick, Dr. Carvell received his degree from the Baltimore Medical School in 1910. He was a member of the American Medical Association.

His widow, two daughters and a brother survive him.

Dr. Leavitt asked the councilors to stand in silence one minute in tribute to the memory of Dr. Carvell. The councilors complied with the request.

Dr. Schadt resumed the chair.

Dr. Donald Munro, Suffolk, moved that the following amendments to the by-laws of the Massachusetts Medical Society be adopted:

That Chapter IV, Section 4, of the by-laws of the Massachusetts Medical Society be amended by striking out the word "stated" and inserting the word "annual" and deletion of the words "in February."

That Chapter VI, Section 5, of the by-laws of the Massachusetts Medical Society be amended by striking out the word "February," as it appears at the top of page 21, and inserting in its place the word "annual."

This motion was seconded by a councilor

Dr. Munro explained that the purpose of these amendments was to allow the Auditing Committee sufficient time to do the job that it was supposed to do under the by-laws. The motion was adopted by vote of the Council.

The President announced that these amendments will be offered at the annual meeting of the Society in 1944 and that they will not be effective until favorably acted on by that body.

Dr. Munro moved the adoption of the following motion:

That the Committee on Publications be empowered to offer to the Navy Department 100 free one-year subscriptions to the *Journal*, to be distributed as the Navy may decide.

This motion was seconded by a councilor.

In connection with this motion, Dr. Munro said that he was offering it at the request of Dr. John Fallon, who was ill and consequently could not be present. He added that he personally favored the motion. He said that he had been informed by the editors of the *Journal* that the adoption of this motion would add but five cents to the cost of the *Journal* for each member per year. He em-

phasized how profitable this would be to the *Journal* from the standpoint of advertising.

Dr. Fitz asked if this had been discussed by the Executive Committee. Dr. Schadt replied in the affirmative and added that the committee had voted against it. Dr. Channing Frothingham, Suffolk, called upon the Council to reverse the action of the Executive Committee.

Dr. Richard M. Smith, Suffolk, favored the motion. He thought from a business point of view it was a good thing to do. He stressed the point that he was speaking as an individual and not as a representative of the Committee on Publications. Dr. Frank R. Ober favored the motion, as did Dr. William B. Breed, Dr. Peirce H. Leavitt and Dr. Donald Munro.

Dr. Carl Bearse, Norfolk, said that this matter had been given very careful consideration by the Executive Committee and that he thought the Council should back up this committee's stand.

Dr. Fitz moved that the motion be tabled and referred once more to the Executive Committee. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

The chair recognized Dr. James P. O'Hare, Suffolk. Dr. O'Hare read a letter from Mr. John M. Deely, district rationing officer, which is as follows:

Owing to the problems that have arisen in the administration of the food-rationing program, we find need of a board of advisors as relating to special diets certified by physicians.

We should deeply appreciate it if the Council of the Massachusetts Medical Society would appoint a committee to assist the state director of food rationing to furnish specific help in formulating a state-wide policy and to pass on doctor's certificates, and to serve as a review committee for unusual cases.

Dr. O'Hare said that many physicians have attempted to help their patients obtain more fuel oil and gasoline than is ordinarily allowed. The problem of food, he added, will be solved by a special federal committee that is now working on this subject. In the meantime the regional director needs help now to solve immediate and pressing problems. Dr. O'Hare moved that the President appoint a committee of three to assist, by advice, the regional rationing board in the problem relating to the special feeding of the sick. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Dr. Maurice Fremont-Smith, Suffolk, was recognized by the chair. He moved "that the President appoint a committee of whatever number he chooses to gather facts on this situation and make a recommendation to the Council." In of-

fering this motion Dr. Fremont-Smith spoke as follows:

Last year the by-laws of the Society were amended so that no foreign physicians coming to this country could get into the Society until after five years in this country. This is no time to go into any discussion. I think there are very good reasons for the Society having taken some action to protect its members against an influx of foreign physicians, many of whom were undesirable and many of whom did not know our methods of practice. On the other hand, there is a considerable body of men in the Society who believe that the Society has done itself no honor by putting this by-law on the book; in fact, we believe that the Society has opened itself to the criticism that it is looking after its own interests rather than those of the public welfare and that it is acting like a medical trust. I know this was not the intention of the Society. There are some arguments against this by-law—whether we should treat all men who come from Europe as one group. I think that that shows little confidence in our local selection boards and in our general election board. I shall not carry this any farther.

Dr. Fremont-Smith's motion was not seconded.

At this point Dr. Schadt introduced the newly elected officers amidst great applause. These officers responded briefly.

The President announced that on Tuesday morning, May 25, 1943, at 9:00 a.m., the scientific sessions of the one hundred and sixty-second annual meeting of the Massachusetts Medical Society would begin.

It was regularly moved and seconded that the Council adjourn. It was so ordered by vote of the Council at 12:00 m.

MICHAEL A. TIGHE, *Secretary*

APPENDIX NO. 1

ATTENDANCE

BARNSTABLE	C. C. Tripp
W. D. Kinney	Henry Wardle
BERKSHIRE	ESSEX NORTH
I. S. F. Dodd	E. S. Bagnall
Solomon Schwager	R. V. Baketel
P. J. Sullivan	H. R. Kurth
	P. J. Look
BRISTOL NORTH	R. C. Norris
W. H. Allen	G. L. Richardson
J. H. Brewster	F. W. Snow
R. M. Chambers	
J. L. Murphy	ESSEX SOUTH
	H. A. Boyle
BRISTOL SOUTH	C. L. Curtis
G. W. Blood	R. E. Foss
R. B. Butler	Loring Grimes
E. D. Gardner	P. P. Johnson

A E Parkhurst
O S Pettingill
W G Phippen
E D Reynolds
H D Stebbins
P F Tivnan
C F Twomey

FRANKLIN

A W Hayes
F J Barnard
H L Craft
W J Pelleuter
H G Stetson

HAMPTDEN

F H Allen
E P Bagg
W C Barnes
Eoline C Dubois
Frederic Hagler
G D Henderson
F S Hopkins
E A Knowlton
A G Rice
G L Schridt
G L Steele

HAMPSHIRE

A J Bonneville

MIDDLESEX EAST

J H Blaisdell
R M Burgoyne
C W DeWolf
Richard Dutton
E M Halligan
R W Layton
M J Quinn
R R Stratton

MIDDLESEX NORTH

H R Coburn
R L Drapeau
A R Gardner
W F Ryan
W H Sherman
M A Tighe

MIDDLESEX SOUTH

C F Atwood
E W Barron
W B Bartlett
Harris Bass
J M Baty
W O Blanchard
G F H Bowers
Madeline R Brown
R. W. Buck
E J Butler
J F Casey
B F Conley
H F Day
C L Derick
J G Downing

C W Finnerty
H Q Gallupe
Stanton Garfield
F W Gay
H G Giddings
H W Godfrey
A D Guthrie
Eliot Hubbard, Jr
L H Jack

A M Jackson
F R Jouett
E L Kattwinkel
A A Levi
F P Lowry
A N Makechnie
J C Merrim
Dudley Merrill
C E Mongan
G M Morrison
J P Nelligan
E J O'Brien
Dwight O'Hara
S H Remick
Max Rivo
M J Schlesinger
E W Small
H W Thayer
A B Toppan
J E Vance
Fresenius Van Nuy
R H Wells
B S Wood

NORFOLK

Carl Bearse
William Dameshek
Albert Ehrenfried
J C V Fisher
Susannah Friedman
David Glunts
J B Hall
R J Heffernan
I R Jankelson
C J Kickham
C J E Kickham
D S Luce
C M Lydon
T F P Lyons
H L McCarthy
R T Monroe
F J Moran
Hyman Morrison
S A Robins
S M Saltz
D D Scannell
Kathleen S Snow
J W Spellman
W J Walton
N A Welch

NORFOLK SOUTH

C S Adams
D L Belding
D B Reardon
H A Robinson
W L Sargent

PLYMOUTH

G A Buckley
P B Kelly
P H Leavitt
C D McCann
J J McNamara
G A Moore
D W Pope
W H Pulsifer

SUFFOLK

H L Albright
A W Allen
W B Breed
W E Browne
F M Chipman
David Cheever
N W Faxon
G B Fenwick
Reginald Fitz
Maurice Fremont Smith
Channing Frothingham
Joseph Garland
John Harmons
L M Hurxthal
C S Keefer
H A Kelly
R I Lee
C C Lund
Donald Munro
H F Newton
R N Nye
F R Ober
F W O'Brien
J P O'Hare

L E Parkins
Helen S Pittman
W H Robey
H F Root
R M Smith
M C Sosman
J J Todd
S N Vose
Conrad Wesselhoeft
C F Wilinsky

WORCESTER

C R Abbott
Gordon Berry
L R Bragg
P H Cook
L M Felton
E L Hunt
E R Leib
L P Leland
W F Lynch
J C McCann
A E O'Connell
R S Perkins
R J Ward
R P Watkins

WORCESTER NORTH

E A Adams
H C Arey
C B Gay
G P Keaveny
A P Lachance
F A Reynolds
J G Simmons
B P Sweeney

APPENDIX NO 2

STATEMENT OF DR HAROLD R KURTZ

I wish to draw your attention to a matter which presented itself to the local membership committee of the Essex North District Medical Society. This matter arose in the course of the examination of one of its applicants for membership in the Massachusetts Medical Society just previous to the last censors' meeting. Having presented the facts in this case, I should like to call on the members of the Council for a sense-of the meeting vote.

An applicant, who is a graduate of the University of Kansas City Medical School in 1932, licensed to practice medicine in Massachusetts in 1937, applied on July 17, 1942, for admission to the Massachusetts Medical Society. His application was sponsored by a reputable member of the profession in his community, and forwarded to the district secretary, together with six letters of recommendation from colleagues of high professional standing in this district. The Essex North local membership committee met, examined and interrogated the applicant very closely and, as a result of that examination and close interrogation, was of the unanimous opinion that he should be recommended for fellowship in the Society. I might state here and now that the local membership committee of Essex

North takes its work very seriously and investigates all applicants, particularly those of unapproved or foreign schools. Unless they meet its unqualified approval the committee does not hesitate to refuse their applications for membership in the Society. This has been amply demonstrated in the past by the number of applicants who have been refused fellowship in the Society.

The chairman of the central committee on membership was duly notified by the secretary that "it is the unanimous opinion of this committee, after due investigation, and close interrogation, that the applicant be recommended for fellowship in the Society." The local membership committee was somewhat surprised when it received word that the central committee on membership did not approve the application, in spite of the fact that it had been unanimously endorsed by the local committee. The reasons given by the chairman of the central committee were that his "educational qualifications were rather dubious." The local committee maintains that it already fully realized that situation, but felt, nevertheless, that it was in a better position to pass judgment on the man's qualifications for membership than was a group of men who in all probability did not know him at all. Furthermore, the local committee felt that his "educational qualifications" would be no different in two years than they were at the present time!

The second reason given by the central committee was "that the local committee was not particularly enthusiastic" and that "his recommending letters were not particularly informative." The local committee, in answer to this criticism, states that it feels that it is not necessary for the local committee to eulogize its applicants, and that when the local committee unanimously approves an applicant for fellowship in the Society, it means exactly that, and nothing else. The recommending letters of the applicant were honest expressions of opinions of physicians of high standing in his district, and due emphasis should be placed on these letters of recommendation.

The third criticism as stated by the chairman of the central committee was that it was of the "greatest importance" that the district membership committee should show "that the district society wants that applicant as a member." To this criticism the local committee replies that the Massachusetts Medical Society is representative of the highest standard of medical practice and medical ethics, and is the organization with which all physicians aspire to become identified. Therefore the applicant seeks the Society, and not the Society the applicant!

The purpose in presenting this matter to you is that it was felt by the Essex North local committee that it had spent a great deal of time in investigating this man's qualifications; it had spent almost an hour in interviewing this man and, as a result, had unanimously approved his application. Yet in spite of all this work, and in spite of the fact that this man was endorsed by a group of men for whom the local membership committee has the highest regard, his application was rejected by the central committee for the reasons which have been discussed above. It is felt

by the local committee that if the opinion of the local committees in general is to be upset by the central committee for such inadequate and unsubstantial reasons, that the function of the local committees will become purely superfluous in character. When Dr. John Monks, of the Suffolk District, introduced the change in the by-laws with reference to application for fellowship in the Massachusetts Medical Society, at the special meeting held on April 9, 1941, he stated, in speaking of the local committee, as follows:

The Committee on Medical Education and Medical Diplomas has sensed for a long time how helpless it was in obtaining adequate information on which to determine the desirability of candidates for fellowship; this point has already been discussed more fully in the formal report. It is believed that a local board will be in every way better fitted to obtain this information than the central committee. The number of men on the board is small, they are already in positions of responsibility in their local society, and two of the three are already members of the board of censors, which eventually will examine those candidates finally approved. Further, it is very definitely felt that in the case of graduates of unrecognized schools the essential responsibility of whether or not they should be admitted to membership in the local society should lie with their own nearby colleagues, not with those farther afield.

He furthermore stated, "The central committee shall take the responsibility of seeing that on the one hand undue pressure has not been brought to bear on the local board to recommend for approval an undesirable applicant, nor, on the other hand, that unwarranted local prejudice bar from approval a desirable applicant." It does seem, then, that the responsibility for recommending or turning down applicants for fellowship should rest with the local committee, under the supervision of the central committee. I might state furthermore, that this was the opinion in the minds of Dr. J. H. Blaisdell's by-laws committee in reviewing the mechanism for application for fellowship in the Society. It is the feeling of the local membership committee of Essex North that the principles, as expressed by Dr. Monks's and Dr. Blaisdell's committees, have been disregarded in this case, and that should this policy be continued, the important work of local committees will be jeopardized and must eventually become purely superfluous.

We have brought this matter to the attention of the Council because we are firmly convinced that the present by-laws for application for membership to the Massachusetts Medical Society are adequate and desirable. An applicant is tried, and approved by his colleagues, who are in an excellent position to know the type of professional ethics which this applicant practices far better than a group of men who in all probability know nothing of the applicant at all! It is hoped that the principles expressed by Dr. Monks will continue to dominate the endorsement of all new applicants to the Society.

APPENDIX NO 3

REPORT OF THE EXECUTIVE COMMITTEE TO THE ANNUAL MEETING OF THE COUNCIL

MAY 24, 1943

The Executive Committee of the Council has just finished the second year of its existence. During most of this time our country has been at war. When the enemy struck at Pearl Harbor, the committee had just about completed its organization. The echoes of this attack had scarcely died when in your name it pledged the skills and treasures of the Massachusetts Medical Society and, if necessary, the lives of its members to the President of the United States in what lay ahead. Pursuant to that pledge, our organization has been called on to make, almost overnight, many most important decisions. Fortuitous then was the circumstance which provided the machinery whereby this was made possible. The committee would have me say to you how greatly it appreciates this privilege of speaking in your name.

The Executive Committee on May 14, 1943, held a five hour session.

It returned, on the recommendation of the Committee on Membership, the following fellows as of January 1, 1943, under the provisions of Chapter I, Section 5, of the by laws:

E. Stanley Abbot, Wayland
 Alice H. Bassett, Boston
 William G. Brooks, Boston
 Charles C. Carroll, Belmont
 Frederick W. Colburn, Hyde Park
 Frank E. Draper, Framingham
 Joseph L. Goodale, Ipswich
 James J. Goodwin, Clinton
 Merton L. Griswold, Uxbridge
 Byam Hollings, Boston
 William F. Patterson, Medford
 Warren D. Ruston, Rockport
 Charles J. Smyser, New Wilmington, Pa.
 Frederick W. Sturt, Dorchester
 Edwin P. Tripp, Falmouth
 Ralph R. Young, Jamaica Plain

It allowed the following fellows to resign as of January 1, 1943, under the provisions of Chapter I, Section 7, of the by laws:

Francis M. Amaral, Point Loma, California
 Joseph E. Cribb, Hartford, Connecticut
 Frances Cottingham, New York City
 Mitchell Gratwick, Tarrytown, New York
 S. Harvard Kaufman, Pittsburgh, Pennsylvania
 Nels A. Nelson, Baltimore, Maryland
 Purcell G. Schube, Pasadena, California
 Joseph C. Stammers, New York City
 Mary Frances Vastine, Philadelphia, Pennsylvania
 William D. Wheeler, Brookline
 Lester R. Whitaker, Augusta, Georgia
 John C. Whitehorn, Baltimore, Maryland

It allowed the following named fellows to change their membership from one district to another without change of legal residence under the provisions of Chapter III, Section 3, of the by laws:

Louis K. Diamond, Brookline (Norfolk to Suffolk)
 Franc D. Ingraham, Brookline (Norfolk to Suffolk)
 Joseph F. Ross, Brookline (Norfolk to Suffolk)

It readmitted the following named fellows who had resigned while in good standing under the provisions of Chapter I, Section 10, of the by laws:

Attilio Canzanelli, Boston
 Arthur H. Crosbie, Boston
 Henry L. Hirsch, Springfield
 Elie J. La Liberte, Springfield

It readmitted the following named fellows, who had been deprived of membership for the nonpayment of dues, provided all their obligations to the Society are discharged within one month:

A. Walter Ciani, Boston
 Patrick H. Walsh, Fall River

It remitted the dues, including those of 1943, of the following named fellows who are ill and incapacitated, under the provisions of Chapter I, Section 6, of the by laws:

Franklin E. Campbell, West Medford
 Harry H. Flagg, Charlestown
 Edwards W. Herman, Lincoln
 Florence H. Knowlton, Placentia, California
 Bernard L. Plouffe, Webster
 Joseph A. Ruel, Haverhill
 Alpha R. Sawyer, Chestnut Hill
 R. M. Shukle, Boston
 William J. Sweeney, Wakefield
 Ruth Weissman, Jamaica Plain

It deprived of fellowship, for the nonpayment of dues, the following named fellows under the provisions of Chapter I, Section 8, of the by laws:

Gertrude W. Baldwin, Boston
 Chester P. Brown, Swampscott
 J. Lawrence Campbell, Denver, Colorado
 Italia M. D'Argenis, Worcester
 Howard T. Fiedler, Philadelphia, Pennsylvania
 Grace E. Gillis, North Haven, Connecticut
 Max Ginsberg, Salem
 Ruth K. Jens, Brooklyn, New York
 John J. Kerrigan, Fall River
 Morris A. Silberg, Roxbury
 Joseph A. Smith, Athol
 Elizabeth A. Sullivan, Cambridge
 Frederick C. Warnshuis, Windsor, Ontario
 Richard S. Woodruff, Pittsfield

The committee, in conference with the Committee on Membership, under a directive of the Council given on February 3, 1943, reviewed the matter which had to do with the remission of dues of those members who had entered the United States Army, Navy or Public Health Service and offers the following recommendation:

Fellows of the Massachusetts Medical Society shall not be required to pay further dues during their period of active service in the U. S. Army, Navy or Public Health Service. Those so requesting may receive the *New England Journal of Medicine* upon request and payment of a \$4.00 subscription fee.

The above does not apply to fellows going into active military service during the first year of fellowship in the Society.

The committee reviewed the report of the Committee on Membership in regard to the matter of establishing a junior membership in the Massachusetts Medical Society.

and approves the report and its conclusions. This report will be offered by the Committee on Membership later in this meeting.

The Council referred, on February 3, 1943, to the Executive Committee four recommendations offered by the Auditing Committee of 1943:

That the investment of the Society's funds should be under the direction of a professional investment company.

That the report of the accountant should be more complete and include a list of investment transactions.

That the latter should include a statement that the report of the fiscal year is reconciled with the report of the preceding year.

That the duties of the Auditing Committee be turned over to a businessman trained as a bank examiner.

The officers of the Society, in connection with the first recommendation, engaged in certain preliminary conversations with Mr. R. H. Loomis, of the investment-counsel firm of Loomis-Sayles and Company, 140 Federal Street, Boston. The investment portfolio of the Massachusetts Medical Society was analyzed by Mr. Loomis, and a summary of this analysis is now presented.

Dr. Michael A. Tighe, Secretary
The Massachusetts Medical Society
8 Fenway
Boston, Massachusetts

Dear Dr. Tighe:

It was a pleasure to meet with you and your associates last month and go over the financial problems of the Massachusetts Medical Society. Since that time I have been given the opportunity of going over the present portfolio of the Society with the idea of noting possibilities of improvement of execution or any step that could be considered for better performance. I am advised that you are considering the employment of investment counsel for help in this matter. In going over the report I have had in mind what effect the employment of such counsel might have on the portfolio.

It would appear that Dr. Butler's administration was a very conservative one and succeeded in the main in maintaining dollar value. It is probable that during the particular period in which he operated this was, in the main, a proper objective, and personally I believe he did an exceedingly good job in a difficult period. To be sure he paid for it somewhat in increased work and in a very much reduced income. Nevertheless, his main objective was accomplished.

Without including the three or four purchases made a few weeks ago in the total tabulation, the account totals approximately \$228,000. There are eighty-one separate items averaging less than \$3000 each. It is easy to see how this was brought about when one considers the specific method used. However, I would say that there should be no need of so many items, particularly if one is going to deal exclusively in AAA securities. The accompanying ta-

ble gives an analysis of the securities in the portfolio by type of security:

	PRINCIPAL	PERCENT- AGE OF PRINCIPAL	INCOME	PERCENT- AGE YIELD
Cash:				
Savings banks.....	\$6,380	3.0	\$118	1.85
Other	20,464	9.0	-	-
Note (Boston Medical Library)	19,000	8.5	570	3.00
U. S. Government bonds:				
Short term	14,566	6.5	366	2.51
Medium term.	12,458	5.5	265	2.13
Long term	3,015	1.5	75	2.49
Short term bonds ..	36,244	15.5	997	2.75
Medium-term bonds..	31,943	14.0	1,352	4.24
Long-term bonds.....	46,317	20.0	1,671	3.61
Preferred stocks.....	3,450	1.5	143	4.15
Annuity policy.....	9,167	4.0	183	2.00
Demand loan	25,000	11.0	-	-
	<u>\$228,004</u>	<u>100.0</u>	<u>\$5,740</u>	<u>2.52</u>

You will note that the yield is 2.52 per cent. If you subtract the demand loan of \$25,000, which draws no income, the yield on the fund then would be only 2.82 per cent. This is an exceedingly low, in fact an unnecessarily low, rate of return. I would like to point out that if you should consider following these methods of investment it would be more sensible for you to invest the entire fund in three or four issues of Government bonds, which would average nearly as good a return as you are now getting. If you had only three or four Government issues they would require practically no attention and probably a much smaller safe deposit box. There would be scarcely any bookkeeping and practically no cutting of coupons. By raising the yield of the total fund to 4 per cent, which certainly is not an unduly high rate, you could very considerably increase the income return to the Society, and at the same time pay an investment-counsel fee. In other words, I can see an opportunity in this particular fund of, first, lessening the amount of work that your treasurer would have to do by cutting down the number of necessary issues and, secondly, of so increasing the yield on the fund as a whole as to provide greater income to the Society and at the same time pay an investment-counsel fee.

In advising you to seek a higher rate of return I do not want to convey the idea that I believe in subjecting the portfolio to undue risk. I believe that the fund as a whole should be conservatively managed and that, by all means, maintenance of principal should be your most important objective. In these days when inflationary factors are so rampant, I believe that your board should give consideration to the question as to whether or not you wish to any degree to try to protect your funds from a declining dollar value. In other words, it would appear that it might be highly desirable for you to attempt to maintain the purchasing power of the income of the fund. Thus far, in the operation of the fund this has not been attempted in the least, and perhaps it has been just as well that this policy has been maintained up to this time. On the other hand, it would appear that the element of inflation is strong enough to provide a proper basis for attempting in some small way at least to protect the funds against the ravages of inflation and a declining dollar.

From the above table you will note that 42½ per

cent of the total fund is in cash or short term funds for maintenance of principal this may have been a proper proportion, but it has been paid for by an extremely low rate of return. It is questionable if the nature of your financial problems is such as to require such a large proportion of your funds in such near-cash securities.

I am not going to itemize the entire eighty-one issues because of the fact that they are so homogeneous in quality. They are all, with the exception of not more than half a dozen issues, of a very high grade as can easily be seen from a consideration of their prices and also from their yield. It is noticeable also in the list that there are a good many very high grade municipal bonds. These municipal bonds carry a tax free feature which is highly desirable to an individual having a high income and therefore, a high tax bracket. In view of the fact that your society, however, is not operated for profit you are not subjected to taxes in any case and, therefore, in purchasing municipal bonds you are buying something that you really do not need. Nevertheless you have to pay for it for the reason that such bonds are increased in price by the peculiar demand on the part of certain individuals. As indicated you have no such demand and, therefore, I would point out that such securities are really not suited to your purposes.

In operating this account it would be desirable to know what the nature of your budget expenditures are. It would be helpful to know what you consider essential as a checking balance for such expenditures.

Now in regard to our services that might be rendered to the Society. We would assign a competent consultant who would have charge of this account in the office and who would constantly be in touch with Dr. Hubbard in regard to any possible sales purchases or shifts in the account. The consultant would have available the entire work of our research department, consisting of approximately forty five people. The consultant would take the initiative in getting in touch with Dr. Hubbard although of course, Dr. Hubbard would have available at all times the opportunity of consulting directly with the consultant himself. Our research department has groups that are dealing with industrial securities, utilities, railroads, bank and insurance stocks and municipals, and also it has men who are following the course of money rates, governmental expenditures and the course of industrial and agricultural prices. In recommending purchases and sales the consultant always gives reasons for the suggested action. It would be important for us to deal with one man and I understand that Dr. Hubbard has the necessary power to proceed. I speak of this particularly because I do not believe that we could be of as much assistance if it were essential to deal with a committee. We have had considerable experience along this line and we have always found that the results are clearly better if we can obtain action easily and quickly and this can usually only be done in dealing with one person. I mention this because upon it depends a great deal the success of any possible assistance we might give you. I am enclosing two copies of our usual contract. The fees which you will note on the bottom of the contract are as follows: annual fee, a rate of 0.5 per cent on the first \$300,000, with 0.4 per cent on additional capital.

Other questions concerning our services may occur to you. I shall be very glad indeed to answer any questions which may come up. In the case of the Massachusetts Medical Society, I feel certain that through the years the fund would be greatly benefited from the application of professional investment counsel. We would be very glad to serve you.

Thanking you for this opportunity, I am

Sincerely yours,
R H LOOMIS

The committee recommends the employment of an investment counsel. In offering this recommendation I am directed by the committee to make clear that it does not intend to commit the Society to just one type of investment counsel. The type supplied by banks should likewise be looked into.

The committee in connection with the second recommendation took notice of Chapter IV, Section 4, of the by laws, which reads as follows:

The Council shall elect at the stated meeting in October, on nomination by the President or from the floor, the Auditing Committee, composed of two fellows who are not councilors.

This committee following the close of the fiscal year, shall require by a certified public accountant an examination of the assets and securities of the Society in the custody of the Treasurer, and of the Treasurer's books and accounts.

This committee shall verify the accountants examination and report its findings at the stated meeting of the Council in February.

It is the opinion of the committee that by this section, auditing committees are provided with full authority to insist on the matter set forth in this recommendation. It is furthermore the opinion of the committee that auditing committees should so insist.

In the debate which attended this subject, it was brought out by Dr. Eliot Hubbard, Jr., treasurer *pro tempore*, that usually the books of the Society could not be closed before January 20. Dr. Francis C. Hall, chairman of the Auditing Committee of 1943, emphasized the fact that this being so the time intervening between this date and the February meeting of the Council was too short to enable an auditing committee to do the right kind of job.

The committee with this in mind under the heading of new business, will offer such amendments to the by laws as will provide that the Treasurer's and Auditing Committee's reports shall be offered to the Council at the annual meeting instead of the February meeting.

It was the judgment of the committee that the last two recommendations were covered by the action taken in regard to the first two.

The Council on February 3, 1943, referred to the Executive Committee a recommendation offered by the Committee to Aid the Boston Medical Library. This recommendation would have the Massachusetts Medical Society turn over to the Boston Medical Library the earnings of the Society's Building Fund. Under this directive the committee was ordered to give this matter the attention and study which it deserves and that its report be given at least twenty days before the annual meeting if it is possible to do so. The committee has complied with this order and its recommendations accompanied the call of this meeting. They are as follows:

That the Massachusetts Medical Society acquire the space now occupied by the *Journal of Bone and Joint Surgery*.

That the Massachusetts Medical Society pay to the Boston Medical Library as rent a sum of money, up to \$6500 per annum, for its quarters thus enlarged.

The committee in arriving at its conclusions in this matter took notice that the history of this organization contains many references as to the desirability of a permanent home. It noted that in 1928 a drive for funds for this purpose was conducted and that a sum of \$18,000 was realized. It noted also that in 1929 a joint drive for funds was conducted by the Boston Medical Library and the Massachusetts Medical Society and that the sum of \$180,000 was raised, one sixth of which, or \$30,000, was allocated to the Massachusetts Medical Society as its share.

In 1931 the Massachusetts Medical Society loaned, from this fund, to the Boston Medical Library \$24,703.29 from which it received 4½ per cent yearly up through 1939. The principal on this loan has been reduced, so that today it stands at \$19,000. In 1940 the interest rate was reduced to 3 per cent.

The Society's Building Fund as it stands as of December 31, 1942, is \$63,991.80—the sum of these original amounts raised plus their earnings over the years.

The committee, in its investigations, noted a vote which was passed by the Council in June, 1929, which reads as follows:

ARTICLE I. All moneys or other funds received by the Society for the purpose of obtaining and maintaining a building for headquarters for the Society shall be kept by the Treasurer in a separate fund known as the "Building Fund."

ARTICLE II. Any interest obtained from the investment of said funds may be used as a whole or in part to pay rental for quarters to be used by the Society for central activities.

ARTICLE III. Any interest obtained from the investment of said funds and not used to pay rental as specified in Article II shall be added to the principal of the "Building Fund."

ARTICLE IV. The principal of said funds may be expended only to acquire real property to which the Society shall hold title.

The committee is of the opinion that this vote, while it continues to stand, precludes the possibility of using the earnings of the building fund as a gift.

In arriving at its recommendations in this matter, the committee calls to the attention of the Council the availability, without extra charge, of John Ware Hall, Sprague Hall, the Prince Room and the Supper Room for the activities of the Society, and the ever-increasing use which is being made of these facilities. It points out how important it is that the offices of the *Journal* be contiguous to the library itself. It finds some disposition to regard the present headquarters as a permanent home provided additional office space is made available for the use of the Society in its attempt to better serve its membership. Such are some of the conclusions which have influenced the committee in presenting these recommendations.

In connection with these recommendations, may I read a letter from Dr. William C. Quinby, which came too late to be considered by the Executive Committee but which is presented at the direction of the President.

To the Council of the Massachusetts Medical Society:

The Boston Medical Library through its Board of Trustees has directed me as treasurer to bring to your attention the matter of the facilities which the Library furnishes the Massachusetts Medical Society and the present need for a readjustment of the terms of the agreement now existing between them.

The desire of the Society for more space having been noted, the Library, to this end, has available the space now used by the *Journal of Bone and Joint Surgery*, consisting of a sizable room on the front of the building and a smaller office across the hall. With the addition of these rooms the Society will have at its disposal all the space to the right of the entrance hall on the first floor of the Library building.

In addition to space under permanent occupancy by the Society it is important to point out that the facilities of Ware Hall, Sprague Hall, the Prince Room and the Supper Room, will be, as in the past, at the command of the Society for those of its meetings as need such accommodation. Also, one half the space in the Library's fireproof vault is reserved for the use of the Society.

For these facilities the Library will charge the Massachusetts Medical Society the sum of \$6500 (sixty-five hundred dollars) as annual rental.

A suggested form of agreement is appended.

WM. C. QUINBY, Treasurer
Boston Medical Library

The committee reviewed and approved the report of the Committee on Medical Defense and that of the Committee on Expert Testimony and approved both.

The committee commends the report of the Committee on Public Relations to the attention of the Council.

The Council, on February 3, 1943, referred the matter of supplying the armed forces with the *Journal* to a joint conference between the committee and the editors of the *Journal*. Dr. Nye reported that the Army had already approved of a plan to subscribe to the *Journal*, placing a copy in every Army hospital of twenty-five beds or over. He further reported that this will amount to between 450 and 500 subscriptions. He added that the Navy could use 100 copies. The cost to the Society of the latter would be about \$400. A motion to send 100 copies to the Navy free was defeated.

The Executive Committee, on February 3, 1943, was directed by the Council to consider some method of attendance that would cause councilors to remain until the business of the Council is completed. The committee in this connection recommends that the stated meetings of the Council, other than the annual meeting, convene at 10:00 a.m. and, while there is any business to transact, do not adjourn for lunch until 2:00 p.m.

The committee acknowledges the receipt of a communication from Dr. Charles F. Willinsky et al. of the staff of the Beth Israel Hospital. With the communication is included a protocol governing a plan for the care of the practices of such members of its staff as have or will enter the armed forces. The communication seeks the approval of the Massachusetts Medical Society. The committee recommends that this matter be referred to the War Participation Committee and that this committee report on this matter at the next meeting of the Executive Committee.

The committee, taking notice of the growing importance of anesthesia and the wisdom of encouraging in every way possible those who are engaged in its development, recommends that the Committee on Arrangements be instructed to provide for an exhibit and a luncheon meeting on anesthesia and for the suitable advertising of this exhibit and meeting in the annual meetings of the Society.

The committee received a letter from the National Conference on Medical Service, including a resolution which this body proposes to have offered in the House of Delegates of the American Medical Association at its meeting next month.

Investigation has shown that this conference springs largely from the Middle West. It could seem to be a bit dissatisfied with the scope of the activities of the Bureau of Medical Economics of the American Medical Association. It would substitute for this bureau a committee on medical service to be made up of the president of the American Medical Association *ex officio*, the immediate past president of the American Medical Association, the secretary of the American Medical Association *ex officio*, a member of the Board of Trustees of the American Medical Association, designated and selected by the Board of Trustees, and one member of the American Medical Association elected as hereinafter provided from each of the following nine geographical subdivisions of the United States:

NEW ENGLAND	MIDDLE ATLANTIC	EAST NORTH CENTRAL
Maine	New York	Ohio
New Hampshire	Pennsylvania	Indiana
Vermont	New Jersey	Illinois
Massachusetts		Michigan
Rhode Island		Wisconsin
Connecticut		
SOUTH ATLANTIC	EAST SOUTH CENTRAL	WEST SOUTH CENTRAL
Delaware	Kentucky	Arkansas
Maryland	Tennessee	Louisiana
District of Columbia	Alabama	Oklahoma
Virginia	Mississippi	Texas
West Virginia		Panama Canal Zone
North Carolina		
South Carolina		
Georgia		
Florida		
Puerto Rico		
WEST NORTH CENTRAL	MOUNTAIN	PACIFIC
Minnesota	Montana	Washington
Iowa	Idaho	Oregon
Missouri	Wyoming	California
North Dakota	Colorado	Alaska
South Dakota	New Mexico	Hawaii
Nebraska	Arizona	Philippines
Wyoming	Utah	Pacific Islands
	Nevada	

The resolution provides

The members of the House of Delegates from each of the foregoing geographical subdivisions of the United States shall elect one member of the American Medical Association to serve on said committee three of said nine members shall serve for one year three shall serve for two years and three shall serve for three years the respective terms of office of the nine members first elected shall be decided by lot and thereafter the said terms shall be for three years

each, the expiration date for the first one year term shall be at the next ensuing annual session of the House of Delegates of the American Medical Association, expiration dates for all terms shall coincide with the dates of the regular annual session of the House of Delegates of the American Medical Association.

The resolution defines the duties of such a committee under seven headings:

(1) The making available of scientific facts and data and medical opinion with respect to timely and adequate rendition of medical care to the American people.

(2) To integrate the activities of the Committee on Medical Service with respective state and county committees on like activities.

(3) Establish relationships and cooperation with other allied groups who are likewise engaged in the rendition of medical care, in its various branches, to the American people.

(4) The Committee on Medical Service shall hold at least two meetings per year one shall be held at the time and place of the annual meeting of the House of Delegates, the other meeting shall be held in the City of Washington, D. C., and called at the direction of the chairman, and such other meetings as may be necessary to be called by the chairman upon the written request of the majority of the committee.

(5) The committee shall forthwith and annually thereafter elect from its own membership a chairman and a vice-chairman.

(6) The Committee on Medical Service shall establish and maintain an office in Washington, D. C. and shall further be empowered and directed to employ a full time executive director, who shall act as secretary of the committee, and, whose duties shall be specified by the committee. Such executive director shall be a physician who has been actively engaged in the private practice of medicine for not less than five years during the previous ten years, and furthermore be informed and qualified to act as a liaison representative of said committee.

(7) The Committee on Medical Service is further authorized to hire such legal and administrative help as is necessary.

The resolution adds that the work of this committee shall be supported by an appropriation from the American Medical Association of not less than fifty cents and not more than one dollar for every member.

The communication called on us to instruct our delegates to support the resolution. The Executive Committee reports that it has not sufficient knowledge of this matter to enable it to recommend that our delegates be instructed to either favor or oppose this resolution. The committee recommends that the resolution be referred to our delegates without prejudice.

A list of appointments for the year 1943-1944 submitted by Dr. Roger I. Lee, president-elect, was approved. This list will be read by Dr. Lee later in the evening.

MICHAEL A. TIGHE, Secretary

APPENDIX NO. 4

REPORT OF THE COMMITTEE ON MEMBERSHIP

The suggestion of the Massachusetts State Committee of the Procurement and Assignment Service, of which Dr. Reginald Fitz is chairman, is as follows:

A curious finding has arisen which it seems to me deserves consideration. Approximately 1900 Massachusetts doctors have commissions or have had commissions with honorable discharge in one of the branches of the armed forces. Of these 1900, only 1050 are members of the Massachusetts Medical Society. Of the 850 commissioned officers who are not members of the Society, 200 in round numbers are standard school graduates and not necessarily desirable for the Society to worry about. That leaves a pool of about 650 young men who represent sort of a floating medical population.

In this pool are interns, residents, fellows, junior teachers in medical schools who come here for two to three years and such people. Potentially, in normal times, they represent a valuable part of our medical population because practically all are engaged in full-time work or are active in research or teaching. I raise the question as to whether the Society and the Boston Medical Library might not make some effort to attract men of this type.

Could we not offer some sort of a junior or temporary membership to both organizations at a reduced fee, and would it not be worth while for these organizations to stir themselves up in order to make their work as appealing as possible to men of this type? What is your thought on the matter?

The Committee on Membership initially, on consideration of the above, was very much in favor of the creation of a new form of membership which might be called a "junior membership," rather than a "temporary membership" or an "associate membership," because we already have in the Massachusetts Medical Society a classification known as "associate fellowship," an honorary grouping; but the committee believed the Society should know what need of such membership existed, to what extent such membership would be utilized in the Commonwealth and exactly what privileges and duties would accompany such membership. It was thought that junior membership must be, at least for the time being, confined to physicians who have graduated from approved schools only. From oral contact with some of the trustees of the Boston Medical Library, it developed that a junior membership in both the Massachusetts Medical Society and the Boston Medical Library, at a reduced fee as suggested by Dr. Fitz, was not feasible or workable. Accordingly, the committee has attempted to clarify the establishment of junior membership in the Massachusetts Medical Society alone and not in combination with any other organization.

There can be little doubt that there is a pool of young physicians, largely interns and residents in hospitals, these physicians not being members of the Society. Your committee has attempted to contact such physicians in the major Boston hospitals and some of the outlying metropolitan hospitals. We have found in our conversations with these groups of men that there was not an excitable interest to join the Massachusetts Medical Society at this time. The *Journal* is available to nearly all these men. The internship at present allowed by the

Government is of one year duration only. The majority of men are financially embarrassed. They feel their future is so uncertain that they have expressed little or no interest in junior membership in the Massachusetts Medical Society, irrespective of privileges granted or duties involved. Hence, the need or the utilization of such new form of membership by this particular intern group of physicians seems to the committee to be exceedingly small.

In order to clarify the rights, prerogatives and duties of such membership, if established, Dr. Fitz and the chairman of the committee have communicated with Dr. Olin West, secretary of the American Medical Association, relative particularly to two points, namely, Would junior membership in the Massachusetts Medical Society, applied to young physicians of not more than five years out of medical school and graduates of approved schools carry with it automatically membership in the American Medical Association? Would the American Medical Association grant its journal or one of its publications to such members at any reduced rate under the regular subscription fee of \$8.00 per year?

Dr. West has informed us in writing that there are intern members in the Chicago Medical Society, who have the right to attend meetings only, and that other component societies have established junior memberships for the benefit of young men who have completed intern service and have been licensed to practice but find it difficult to pay regular membership dues. There have also been established a few associate memberships in some state societies, but the number of component societies who have established such classification are few. To quote from Dr. West:

My information is to the effect that not any intern members or junior members or associate members of the kind referred to above are entitled to vote or to hold office and that the names of the members of those special groups are not reported to the secretary of the constituent state medical associations immediately concerned for enrollment as members of the state associations. Associate members of constituent state medical associations *are not* supposed to be reported to this office for enrollment as members of the American Medical Association unless they have all the privileges accorded to active members under the constitution and by-laws of the individual constituent state medical associations immediately concerned.

Dr. West further states that it is improbable that the journal or one of the other American Medical Association publications could be furnished to any physicians at less than the set cost of \$8.00 per year.

It is therefore clear that junior membership would not carry automatically membership in the American Medical Association.

The committee further believes that it would be impossible to establish a junior membership on any financial basis less than that commensurate with the cost of the *Journal*. It seems obvious that such membership would not allow the holding of office but would carry with it attendance and participation in the meetings of the Society.

Bearing in mind the results of its investigations, as briefly outlined above, the Committee on Membership favors in principle the establishment of a junior membership for physician graduates five years or less of approved medical schools, but does not think that this

is the time for the establishment of such new class of membership because of unsettled war conditions

HARLAN F. NEWTON, Chairman

APPENDIX NO 5

REPORT OF THE MASSACHUSETTS STATE COMMITTEE OF THE PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS

The Massachusetts Medical Society may well feel proud of the record already made by young Massachusetts doctors in the present war.

Captain Edward Mozes, of Malden, was in the fighting at Guadalcanal. He was a battalion medical officer, responsible for collecting the wounded of his unit, caring for them as best he could, and for evacuating them. The country was hilly, in ridges, dipping in and out of steep and treacherous ravines, so that all medical equipment and supplies had to be carried by hand. The enemy was within easy range, pestering our men with machine gun fire, mortars, artillery and sniping. Captain Mozes organized his detachment effectively under these circumstances, he performed a leg amputation and gave plasma to a number of patients in the field, he developed a small advanced hospital for the immediate treatment of those who developed malaria, and when ever his battalion moved he always was in column with his men, ready to handle any emergencies that might arise. Clearly, he set an unusually fine example of intelligent and fearless work in very trying conditions.

Lieut. John T. Roach, of Jamaica Plain, was a medical officer on the *Lexington* in the Coral Sea. With utter disregard for his own personal safety he treated the wounded on his ship and directed the removal of casualties from a dark and smoke-filled compartment frequently shaken by violent explosions. His outstanding conduct, his cool courage and his professional skill undoubtedly saved the lives of a great many men who must inevitably have perished without his assistance.

In French Morocco, Lieut. Charles P. Roberts, of Boston, another naval medical officer, administered plasma to a severely wounded soldier under direct shell fire and bombing. As in the case of Lieut. Roach, he too appeared entirely unconscious of his own safety as he carried on his work.

One reads, with great respect, such reports of the gallantry which our young men are displaying, because although these isolated episodes happen to have been described in the newspapers, they are typical of what our medical officers are doing quietly and inconspicuously wherever there is need.

Hearing that there were a number of wounded men lying in front of his Aid Post, this officer went forward under heavy shell fire and, regardless of his own personal safety, attended to them. By his action and bravery the lives of many men were saved.

This was said in 1918 of one of the present members of the Council. It gives a feeling of pride to know that our young medical men of today are chips of the old block and that they are upholding the traditions of medical service which have been passed on to them by their seniors.

Editorials have appeared in the *Journal of the American Medical Association* and the *New England Journal of Medicine* recently, commenting on the urgent and immediate needs for more officers from this part of the country. Whether one agrees or disagrees with the computations involved is beside the point. The fact remains that the Army and Navy are asking for more medical officers.

The 1942 *American Medical Directory* credits Massachusetts with 8085 doctors. Of these, the Society claims as members 5351. Thus there are two distinct pools of medical men in the State—those who belong to the Massachusetts Medical Society and those who do not.

The latter group comprises 2734 physicians. In this pool are young men who are graduates of medical schools approved by the Surgeons General but who have not applied for admission to the Society, a number of graduates of substandard schools who are ineligible for membership in the Society under our present by-laws but have obtained commissions, a residue of older physicians for whom the armed forces have no need, and a group of younger men who are licensed to practice medicine in Massachusetts but are not commissionable for a variety of reasons. This particular source of medical officers is now nearly used up. It appears to have yielded 1269 officers and cannot be expected to supply many more.

Officers to be commissioned in future, therefore, must be derived almost entirely from the ranks of our own membership except in the case of the very young men who are commissioned as medical students. These men, as they complete their internships, will enter the armed forces automatically.

The War Manpower Commission talks in terms of ages, grouping doctors under thirty-eight years old in one class, those between thirty-eight and forty-five in another, those between forty-six and sixty-four in a third, and those over sixty-five in a fourth. In a war such as the present, doctors who are most youthful make the most desirable officers. A sampling of the age of 1900 medical officers drawn from Massachusetts shows that 67 per cent were under thirty-eight years old, 22 per cent between thirty-eight and forty-five, and 11 per cent were between forty-six and sixty-four. Another way of saying this is that in the medical corps of the Army and Navy the youngster in his early thirties is encountered six times as frequently as is the venerable old man of fifty, and three times as often as is the middle-aged doctor in his forties. The chances are, too, that, on the whole, in warfare the medical man's usefulness is inversely proportional to his years.

We have in the Massachusetts Medical Society 1269 (24 per cent) doctors under thirty-eight years of age, 1128 (21 per cent) who are between thirty-eight and forty-five, 2032 (38 per cent) who are between forty-six and sixty-four, and 891 (17 per cent) who are more than sixty-five. The distribution of age groupings varies to a certain extent in the different districts, although the general trend is identical, universally among our members there are more older men than younger men.

A graph has been constructed which shows how the members of the Society in different age groups have been classified by your committee (Fig. 1). Nearly every member in the Society has now been labeled 'available' or 'essential', and in the case of the 'availables', as being in one of the services, or having been rejected as unfit.

for military service by one of the surgeons general, or as still being potentially commissionable.

The forty-five-to-sixty-four group can be dismissed very promptly. Men in this age group who wish to volunteer are likely to do so, and it makes little difference to them who wishes to call them essential. On the other hand, except in occasional instances, their services are unlikely to be more useful in the Army and Navy than

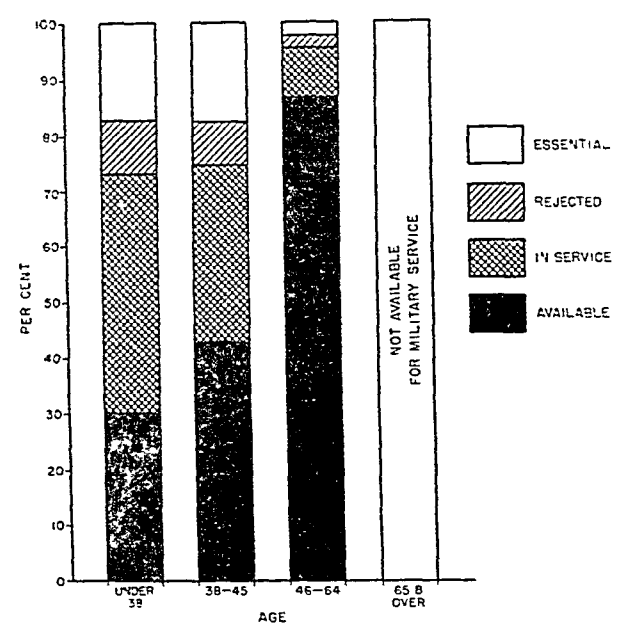


FIGURE 1. Analysis of the Membership of the Massachusetts Medical Society.

in civilian life, and neither branch of the service will put any pressure on men of this age to join.

Doctors in the age group between thirty-eight and forty-five are more problematical. To be sure, as already stated, they are likely to be less useful, by and large, than younger men, but on the other hand, they still can make very desirable officers. They are apt to find it a difficult matter to uproot themselves from civilian life for they are well established. Many are qualified specialists. One of the important pieces of work to be done will be to analyze each of the availables in the group in our membership with a view of determining how many and which ones should be encouraged to volunteer.

The youngest age group, those doctors under thirty-eight years old, are the ones most keenly sought by both Army and Navy. The majority of doctors from Massachusetts who enter the Army or Navy during the next few months should come from it, and it is here that are encountered many perplexing problems. Here are men who have been called essential and, whether justifiably or not, may require investigation. Here, in any city or town, is the residue of available men who appear to become increasingly essential as time goes on, whereas had they obtained commissions earlier nobody would have noticed their absence. Here are encountered patriotic young men and themselves weighed down by a variety of family problems and need advice regarding things to do.

Another graph has been constructed which reveals the uniformity with which the different districts have supplied medical officers (Fig. 2). It is apparent that our members have gone into the Army and Navy from the

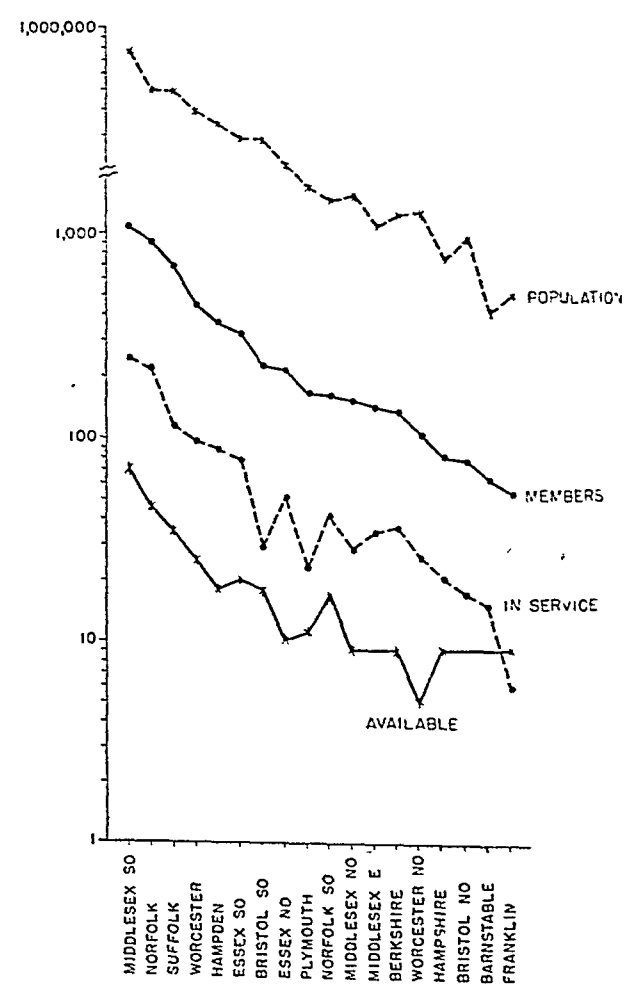


FIGURE 2. Graph to Show the Manner in Which the Different District Societies Have Supplied Medical Officers. The ratio between population, membership and officers supplied is relatively uniform.

different districts in about equal proportions and that so far local Procurement and Assignment committees have used nice discrimination in avoiding any serious medical depletion. The problem that remains is to determine how many of those left in each district should be pressed into national service. Obviously, the largest numbers must come from the largest district societies.

On the ratio of doctors to population we still have more doctors than we need. Although a number of our young men have left the State, the health of the people does not show evidence of having been injured thereby. Nor does the additional load of work thrown on the older physicians who have stayed behind appear to have been harmful. During 1940, 1941 and 1942, the Society lost each year by death about a hundred members, and during the last twelve months only seventy-five. Thus Massachusetts seemingly can spare more doctors.

Since the last meeting of the Council a plan to accelerate enrollments has been proposed by the War Manpower Commission. Stated briefly, the plan, as it might be adopted here, is as follows:

Henceforward, a physician who is declared available to apply for a commission and does not do so will receive written notification from the Massachusetts Medical Society in these words:

Dear Doctor

You have received notification from the Procurement and Assignment Service for Physicians of the War Manpower Commission that you have been declared available and inviting you to apply for a commission. You are requested to appear at _____ on _____ when your case will be reviewed by a committee of the District Medical Society.

Each district medical society will be asked through the President of the Massachusetts Medical Society to establish a reviewing committee. This committee will be composed of older men of unquestioned impartiality and character. One of them will serve as presiding officer of the committee, and another will act as secretary and recorder. The president of the district medical society, the president of the Massachusetts Medical Society and the chairman of the local Procurement and Assignment committees will be members of such reviewing committees *ex officio*.

Such committees will attempt to interview all available men in each district as the names are submitted, explaining the need of the armed forces for medical officers and a physician's obligation to volunteer. If a doctor does not wish to volunteer, for any reason, the committee will hear his arguments. If the committee believes that a man classified as available should not enter the armed forces, it shall say so; or on the other hand if it believes that a man should volunteer, it shall so inform him. The recorder of each committee will keep the chairman of the War Participation Committee of the Society informed of its decisions, and the latter committee will in turn report to the Massachusetts State Committee of the Procurement and Assignment Service for Physicians. Final opinion as to a man's availability will continue to rest in the Corps Area Committee.

If a man declared available does not apply for a commission within ten days after his case has been considered in this fashion he will be reported to the state director of Selective Service, with a request for his reclassification.

This plan, which amounts to establishing a mechanism for the direct solicitation of medical officers by the Massachusetts Medical Society through each of its district medical societies, offers the threat of possible depletion of medical manpower from overzealous recruiting. Your committee believes, however, that the plan can be made to operate safely and effectively.

Your committee, therefore, begs leave to conclude this report with the following resolution:

WHEREAS The War Manpower Commission has announced that there is immediate need for more physicians to serve as medical officers in the armed forces of the United States, and

WHEREAS The War Manpower Commission has announced that Massachusetts should supply more medical officers than have so far been commissioned from the State and

WHEREAS A plan has been suggested by the War Manpower Commission through which the enrollment

of medical officers may be accelerated with the help of county or district medical societies in certain states, therefore, be it

RESOLVED, That the Massachusetts Medical Society support this plan, and be it further

RESOLVED, That reviewing committees be established by each district society, the members of which shall be nominated by the district society presidents and appointed by the president of the Massachusetts Medical Society. Such committees shall serve for the general purposes outlined in this report.

REGINALD FITZ CHURCH

APPENDIX NO 6

REPORT OF THE COMMITTEE CONCERNED WITH PREPAYMENT MEDICAL CARE COSTS INSURANCE

Carrying out the understanding that I should bring periodic reports of progress, I present an interim report utilizing the time given to the Committee Concerned with Prepayment Medical Care Costs Insurance.

I shall first discuss the present status of Massachusetts Medical Service. There is, of course, the question, which is always pertinent as to the desirability of the present time for starting such a program. There is a difference of opinion on this matter. The State Department of Insurance believes that this is a favorable time, but other groups maintain that owing to the change in the economic status of the working family, this is not a desirable time. However, an attempt to present the program effectively to the public has been started in recent months. In January there were a few samplings in the Boston area. It is only since the last week in February that an effort to sell the whole state was undertaken. Since a few months are needed to begin the work of interesting groups before a sales campaign can become effective, it really means we are just starting underway to procure subscribers.

There are different factors which bear and will bear on the growth of this organization and I just want to outline them as quickly as I can under four headings. If you carry these headings in your mind, it will give you a better grasp of our problems. The first relates to the whole organizational activity; the second relates to the type of contract; the third relates to sales problems; and the fourth relates to income limitations established by the Society.

Regarding organizational activities there is a matter which is known to the voting members relating to the \$75,000 which the Council so generously voted and made available to the corporation. The Commissioner of Insurance ruled that only \$5,000 of that shall be available to start the corporation and that \$70,000 shall be held by a bank in trust, to be used only with his approval in a letter bearing his signature and when we have a surplus of \$25,000. So that you can see we are really starting in under a very definite handicap and I feel that the Council should know that \$20,000 of the \$25,000 is retained in the bank earning interest. Then there is the requirement that out of first year premiums a 25 per cent reserve shall be set aside. This is not available either for meeting the expenses of the corporation or for paying the physicians. In the face of these facts it is very evident that we can work only to a certain point at which premiums must begin to grow adequately to carry us along.

Regarding another angle bearing on that point, we have been working in close co-operation on a contract basis with the Blue Cross. Much of the \$5000, as you must realize, has been used up in the initial printing and miscellaneous expenses incidental to starting the program. Outside of that, there has been the contribution of a tremendous personal effort by the members of the Blue Cross organization. That effort has been given most generously, but it is very evident that there is a point beyond which we cannot pass, so far as that personal contribution is concerned. The question has not yet been raised, but certainly it is common sense that our premiums must begin to accumulate to that point where they will meet the percentage requirement that will be due the Blue Cross group for sales effort and organizational activities. Certainly that is not in sight yet.

The problem of sales is definitely related to the fact that the salesmen of the Blue Cross organization have only a limited amount of time that they can give to the Blue Shield program. In order to augment the growth of the Blue Shield a quota has been established for the salesmen. For the Blue Cross their monthly quota shall be 500 subscribers; and 100 for the Blue Shield. With this quota basis it is hoped there will be increased effectiveness in selling the Blue Shield program.

Among the organization activities there is the question of reaching the profession. We have at the present time 4500 men in the state in active practice, and it is a difficult problem to get all information to them so that they can effectively understand it and make up their minds whether they are going along with the program. The chief approach in the past, as you know, has been personal—last year through speeches to the county societies, and then through the distribution of information to the members of the Society in the form of statements in the *Journal*; there has also been some degree of publicity in the papers. At present it is difficult to carry on much publicity because of the fact that there is not a great deal of sales achievement to which publicity can be related. Also, with reference to the profession is the very pertinent problem of the nonacceptance of the corporation by some doctors, which is related to several very evident facts. First, there are groups of physicians who have not become persuaded that the prepayment plan offered by the Medical Society is a necessary program. Then there is a group which questions the type of contract, feeling that the basis of surgical and obstetric coverage is not broad enough. Third is the nonacceptance of the fee schedule by a definite proportion of the men. Then there is the fact that some of the men who are nonparticipating physicians hinder the sales of contracts to prospective groups by reason of their own nonparticipation.

The second factor is the type of contract. I shall not go into it extensively, but it requires brief reconsideration. There are, of course, only three definite approaches possible on the present basis of experience. One is the complete medical-care contract, another the complete hospital coverage, and the third is surgical-obstetric coverage in the hospital. As you look across the country you see that there has not been a successful move by a state medical society to offer a complete-coverage contract. Oregon is the only one at present which is active in this respect, but on a county basis. Others have moved away from it even to the extent of giving up their program of complete service coverage and adopting surgical-obstetric programs on a cash-indemnity basis. There has been some renewal of interest in Cali-

fornia and Buffalo in complete coverage simply because of the fact that the Government is participating with the medical groups in starting such service to cover war industries and housing projects. The complete hospital coverage so far is being undertaken only by New Jersey; it was tried and given up in Buffalo. The number of policies of this character sold do not indicate yet any increase in interest as compared with a surgical-obstetric contract. Concerning the latter, with which we have started, it is unfortunate that, since in other states 69 per cent of payments are to general practitioners, it has been misinterpreted through the state as a specialists' program.

Regarding the third factor, the sales program, there is one big item of importance which enters into the problem so far as the support of the profession is concerned, and that is that experience across the country shows that in order to avoid financial difficulties with the program a very definite percentage requirement is needed to enroll any single group. This ranges from 50 to 75 per cent. We are attempting to liberalize some of these requirements. But it is well to keep in mind that lacking care we can repeat the experience of a large state on the western coast, where the program has cost them already \$100,000; and in Michigan the deficit was, until recently, over \$500,000. They have gradually reduced this to \$365,000. Nonparticipation by physicians may limit the appeal of the program so that it will be difficult to meet percentage requirements.

With regard to the fourth factor, the problem of the limitation of incomes, that relates particularly to the change in status of the workmen in the state. We established the income limitation for the service benefits, that is, no extra charge by the physician, at \$2000 for the individual and \$2500 for the family. A recent report on this state shows a marked increase in the average earnings in certain districts, so that the question of whether we can procure a cross-section enrollment is before us. The average income today in the state is \$41, which makes an income of \$2050 for the year. When we check that against the percentage requirement for enrollment of certain groups, it is questionable whether the percentage can be procured. In certain sections it would seem too many workers would be out of the picture. That is so with the \$49 weekly earnings average which now applies to Beverly; and in Worcester, the average income is \$47 per week. As I evaluate the service offered and the problem of enrollment percentages, those in the low-income group may not enroll; the high-income group does not seem to be keenly interested in cash indemnity without protection; and the middle-income group, the group earning from \$2000 to \$2500, is not now a large enough group to meet the percentage requirements for enrollment.

The question will arise, if the present situation continues, whether the Society should consider doing something with reference to the income levels. There are only three possible approaches other than maintaining them at their present levels or increasing them slightly, say to \$3000 for the large family. One is that there be no ceiling, as in Oregon and Buffalo. The other is to have a second higher premium structure and fee schedule for upper-income groups. That is like Dr. Elliot's plan in New York, which has not yet been very effective. The third is that the Society might consider the question of adding to the present service base an arrangement for a fixed additional charge—a ceiling charge over and above

the fee schedule applicable to the \$4000 or \$5000 groups, beyond which they would agree not to go. Finally, a reconsideration of a ward contract discussed in committees but not presented to the Council will be called for in the future.

I simply call these facts to your attention for future consideration. They may present serious questions depending on what happens to the program in the light of experience in the next few months. As a basis for recommendation I should first simply suggest that this present setup be given a thorough trial, as far as the sales effort is concerned, for several months, and that we keep close watch to determine whether or not it is beginning to carry itself on the basis of contracts sold and premiums earned. Then if any change is desired it should be definitely related to a careful study of experiences elsewhere and an evaluation of the validity of those experiences as they are related to our state program. If possible we must seek to procure more definite co-operation and understanding by the profession through continued approach to them so that all may understand how vital it is for us to achieve success with this program.

JAMES C. McCANN, *Chairman*

APPENDIX NO 7

REPORT OF THE COMMITTEE ON CANCER

Your interim chairman of the Committee on Cancer is deeply sensible of the honor which appointment to the position so long and so ably filled by Dr. Shields Warren has conferred upon him. Having held this office but a few weeks, his report can hardly be as comprehensive as could be desired; nevertheless he wishes to report the work of the committee to date. It was not possible to file the report for prepublication because of the shortness of the interval between appointment and the time the report was requested by the Secretary.

A meeting of the committee was held at the Hotel Sheraton Boston, on May 7. Drs. Simmons, Truesdale, Daland, and Hunt were present.

A hearing was given to Mr. H. D. Fish, assistant managing director of the American Society for the Control of Cancer, Incorporated, who presented a plan for lay organizations in the large centers of population to extend the work of popular education in co-operation with the state program and backed by the experience and facilities of the Society. After free discussion, the committee decided that it was inexpedient to launch the suggested plan at this time.

Dr. Herbert L. Lombard, director of the Division of Adult Hygiene, Massachusetts Department of Public Health, was present by invitation and submitted the following statement in regard to the educational program of the department:

The exigencies of war have seriously interfered with the cancer education program in this state. This is particularly true concerning the activities of the co-operative cancer-control committees. The absence of many physicians, the scarcity of gasoline and the inherent dangers of the blackout have resulted in a greatly diminished number of cancer meetings. The realization that the situation might become more acute, combined with the need for a continuation of some type of cancer education during the period of war, prompted a two-day symposium to discuss means and methods of carrying on the educational campaign.

The participants in the symposium included Professor Edwin B. Wilson, Dr. Shields Warren, Dr. Ernest M. Daland, Dr. Ira T. Nathanson, Dr. Clifford C. Franseen, Dr. Ernest L. Hunt, Mr. Ernest Stephens, Mr. Richard J. Schmoey, Mr. Winthrop L. Webb, Mr. George L. True, Mr. W. O. Johnson, Mr. Arthur D. Thomson, Mrs. Florence Parker, Mrs. Dorothy Averhill, Miss Margaret Allen, Mrs. Hilda LaRocca, Miss Mary M. Hurley and other members of the staff of the Division of Adult Hygiene, Department of Public Health.

As a result of the symposium a booklet, *Cancer: The what, whether, how*, has been prepared which can be used either by the co-operative cancer-control committees or by schools desirous of helping in cancer education. A monthly bulletin, *Cancer Tidings*, is being sent to the central committees, both to maintain their interest and to further cancer education. In so far as possible the regular talks of the co-operative cancer-control committees have been given but there has been a distinct decrease in their number.

The cancer situation in Massachusetts, however, improved in 1942. The interval between first symptoms recognized by the patients and consultation with the first physician was the lowest it has ever been. The adjusted death rate for females again dropped and has now returned to the level of 1913.

It is very gratifying to record the continued interest of so many people in the cancer program in spite of their many other activities.

Dr. Channing Simmons reported on state-aided cancer clinics, particularly in relation to the changes and progress growing out of the survey which he conducted last year, the details of which were reported to the Society through the *Journal* (September 17, 1942) and formed part of the report of this committee at the October meeting of the Council. In that report he criticized seven clinics and made certain suggestions which have been carried out, so far as possible by the Department of Public Health. The Quincy Clinic has been discontinued. The Newburyport Clinic is essentially combined with that of Beverly at least for the duration of the war. The Hyannis Clinic is unsatisfactory. The attendance has fallen off lamentably since the shortage of gasoline. One surgeon strives to keep it going because it is geographically important and affords a limited opportunity for carrying on educational work. The Pittsfield Clinic was discontinued by vote of the local medical society. This is unfortunate considering the geographical situation of the city. Transportation to Westfield is good. However, reorganization of the Brockton Clinic by the Plymouth County Cancer Committee has taken place, and it is now conducted on lines very closely approximating the standards defined by the Department of Public Health. It is the belief of clinic chief, Dr. G. A. Moore, that changes effected will make for more efficient service to an increasing number of patients. Concerning the Greenfield and Springfield clinics details on which to base an estimate of progress from the situations considered unsatisfactory in the 1942 survey have only today come to hand and show definite gains since the date of the survey.

All the clinics suffer from losses to the armed services of staff personnel but are carrying on as best they can. Many older men have taken over the work of their

younger colleagues, and volunteer nursing and clerical aides have helped in those phases of the clinic service.

In spite of the handicaps imposed by wartime conditions it is believed that there must be no letup in the cancer-control effort. It is the opinion of your committee that a greater awareness of his opportunity on the part of every individual physician practicing in the State could do much to offset the loss of trained workers in the clinics. Such awareness should be acquired by the physician by drilling himself in the habit of requiring the completion of a diagnosis in all cases that present any symptom or sign which may by any possibility be due to cancer. Definitive diagnosis without undue delay is the desideratum. Nothing less can square with the doctor's sense of duty to his patient.

Fortunately such are the standards of most doctors. The progressively shortening intervals between the time of seeking advice and the receiving of definitive treatment as revealed by the experiences of the state clinics shows that physicians are more and more generally living up to the demands of the situation and are, moreover, taking active part in spreading the gospel of early diagnosis through personal contact with their families and by talks to lay groups which now abound in every community.

As the medium through which the benefits of modern medical science shall become available to the individual citizen it is our conviction that there is no substitute for the well-educated, experienced, conscientious doctor.

ERNEST L. HUNT, *Chairman*

APPENDIX NO. 8

REPORT OF THE MILITARY POSTGRADUATE COMMITTEE

The Military Postgraduate Committee held its first meeting on November 6, 1942, when plans were made to provide postgraduate extension courses for the Army and Navy medical officers who are stationed within the Commonwealth. Colonel J. J. Reddy, chief of medical operations of the First Service Command, and Captain H. L. Kelley, chief of medical operations of the First Naval District, had already welcomed the offer of the Society and advised the committee to proceed to arrange a curriculum and organize a teaching staff. At this meeting the committee conferred with officers representing the medical staffs of Fort Banks, the Chelsea Naval Hospital, Camp Edwards, Fort Devens, the Portsmouth Navy Yard and Westover Field. As a result, a curriculum was developed and a faculty organized. The plan of postgraduate instruction included clinics and ward rounds with the instructor acting as a consultant, supplemented by formal and informal lectures.

The committee is unanimous in reporting that this project has been well worth the effort and expense. Much has been learned in regard to the postgraduate needs of the medical officers of the armed forces, as well as about the methods of presenting the subject matter. Each session has been an ordered military formation, so that the attendance has been practically 100 per cent. Our civilian instructors have learned that punctuality and thorough mastery of the subject matter are necessary to meet the exacting demands of wartime medicine.

On May 20, 1943, the committee held a second joint meeting with representative medical officers from the various Army and Navy posts. The work of the past winter was reviewed; constructive criticism was received from each of the medical officers present. The committee's work has been greatly facilitated by comments and suggestions from these officers during the past season. Some of their comments will be of interest to the Society.

Westover Field. Colonel Schwichtenberg and Lieutenant Staples report that clinical case teaching and informal ward rounds at the Station Hospital before the lectures have helped greatly in holding interest and making the teaching more practical. They consider the course highly successful and heartily thank the Society for providing this postgraduate program.

Camp Edwards. Lieutenant Colonel John C. Eckels and Lieutenant Colonel Lewis W. Hill gave an enthusiastic account of the postgraduate courses at their camp. They find that the time spent in going to the postgraduate programs is very much worth while. They wish to inform the Society that a camp commanding officer may detail any medical officer for ten days' residence instruction without cost to the Government at any time; they hope that the committee will find it possible to provide for such residence postgraduate instruction during the coming year. They expressed the appreciation of all their medical officers for the work of the instructors.

Fort Banks. Major R. Earle Glendy gave a review of the postgraduate courses offered at their hospital; the interest has been above average, and they request a continuation of the courses on a year-round basis, if possible.

Portsmouth Naval Hospital. Commander Eugene H. Drake reported that they greatly appreciated the courtesy of the Society in sending an instructor to their hospital and hoped further prograduate instruction could be provided for the Navy.

Lieutenant Commander James M. Faulkner, of the Chelsea Naval Hospital, cited the large naval hospital at the Quonset Air Base in Rhode Island and asked if the Society could be persuaded to offer instruction there.

Fort Devens and the Chelsea Naval Hospital have been handled by members of local medical societies; since these programs had already been arranged, your committee had nothing to do with them officially, although several of our instructors attended the meetings. The officers at these posts report that they will probably use the Society's teaching facilities another year.

The committee had a budget of \$350; \$235.07 has been spent for necessary expenses, leaving a balance of \$114.93. Both the Army and Navy extend their thanks to these busy teacher physicians who donated their time.

The medical officers in charge of the postgraduate courses are as follows: Fort Banks, Major R. Earle Glendy; Chelsea Naval Hospital, Lieutenant Commander James M. Faulkner; Fort Devens, Colonel Gilbert T. Hyatt; Camp Edwards, Colonel C. W. Riley; Lieutenant Colonel John C. Eckels and Lieutenant Colonel Lewis W. Hill; Portsmouth Navy Yard, Commander Eugene H. Drake; Westover Field, Colonel Albert H. Schwichtenberg and Lieutenant Charles Staples.

Twenty seven instructors gave a total of thirty three sessions as follows:

DATE	SUBJECT	INSTRUCTOR
FORT BANKS		
Nov 13	The Importance of an Unstable Blood Pressure in Applicants for Military Service	Dr Robert W Wilkins
Nov 20	The Importance of Renal Glycosuria in Applicants for Military Service	Dr Howard F Root
Nov 27	The Management of Peptic Ulcer Patients	Dr Franklin W White
Dec 11	Blood Plasma as a Therapeutic Agent	Dr Charles A Janeway
Jan 8	The Early Recognition and Treatment of War Neuroses and the Common Psychoses	Dr H Houston Merritt
Jan 22	The Acute Abdomen	Dr Hollis L Albright
Feb 19	Chest Injuries	Dr John W Strieder
Mar 5	Vitamins with Special Reference to Surgical Patients	Dr Harold Jeghers
Mar 19	Surgery of the Neck	Dr Herbert D Adams
Apr 2	Genitourinary Infections	Dr Oscar F Cox
Apr 23	Chemotherapy	Dr Howard Allen

CAMP EDWARDS

Nov 23	Hypertension	Dr Laurence B Ellis
Dec 17	Surgery of the Neck	Dr Richard B Cattell
Dec 30	Atypical Pneumonias	Dr Maxwell Finland
Jan 14	Emergency Abdominal Surgery	Dr Samuel F Marshall
Jan 28	Back Pain and Foot Trouble	Dr William A Rogers
Feb 11	Syphilis	Dr Francis M Thurmon
Feb 25	Blood Diseases with Particular Reference to Blood Infections	Dr William Dameshek

Mar 11	Shock	Dr Stanley Bradley
Mar 25	Peripheral Vascular Surgery	Dr Reginald H Smithwick
Apr 8	Head and Spine Injuries	Dr Donald Munro

PORTSMOUTH NAVY YARD

Dec 17	Pneumonia	Dr Maxwell Finland
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WESTOVER FIELD

Dec 3	The Acute Abdomen	Dr Richard B Cattell
Dec 11	The Problem of Head Injuries and Their Treatment	Dr Donald Munro
Dec 30	Low Back Pain and Foot Trouble	Dr Frank R Ober
Jan 13	The Nature and Treatment of Congestive Heart Failure	Dr Samuel A Levine
Jan 27	Atypical Pneumonias	Dr Chester S Keefer
Feb 10	Genitourinary Infections	Dr Oscar F Cox
Feb 24	Burns	Dr Donald W MacCollum
Mar 10	Internal Fixation of Fractures	Lieut Clarke Staples
Mar 24	Chest Injuries	Dr Richard H Overholt
Apr 7	Blood Transfusions	Dr William Dameshek
May 19	Treatment of Knee Injuries	Dr Frank R Ober

The committee recommends.

That the committee be continued and directed to enlarge its activities so far as practicable

That an invitation be extended to the other New England state medical societies to co-operate in this project and that all medical officers of the Army and Navy in New England be offered postgraduate instruction in some form

That the Massachusetts Medical Society underwrite the expense of this effort

W RICHARD OHLER, *Chairman*

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 29271

PRESENTATION OF CASE

A twenty-nine-year-old woman was admitted to the hospital because of back pain and an abdominal mass.

Seven and a half months before entry, one month after the birth of an only child, the patient, when wearing a girdle or when leaning against a solid object, noticed a throbbing sensation in the left lower quadrant, which was synchronous with the pulse. The pregnancy was her first, and was not remarkable except that during the last five days of the puerperium urinary retention was severe and required catheterization. The delivery was at term and was uneventful. Following delivery she suffered with extreme fatigability, her habitual constipation increased and nausea developed. Four months before entry, one week prior to catamenia, a severe aching pain developed in the mid-dorsal region that was intermittent during the day and constant during the night, often interfering with sleep. Before and during this catamenia, which was normal in amount and duration, she had severe abdominal cramps that made her double up. She had never had premenstrual or menstrual distress. Subsequent periods were entirely normal. At that time she felt a small firm nontender mass in the left lower quadrant. Three weeks before entry the mass increased in size and gradually rose higher in the left side of the abdomen. During the three weeks prior to admission the back pain became progressively worse and the patient was obliged to sleep in a sitting position. She gave up the use of proprietary laxatives because of the great exacerbation of pain that these produced. Her physician confirmed the presence of a mass in the left side of the abdomen. At the time of admission she was troubled by weakness and back pain. At no time had there been any menorrhagia, metrorrhagia, hematuria or pyuria. Despite continuous nausea she had vomited only once in eight months. She had never been jaundiced. The stools had never been tarry, bloody or acholic, nor was the urine dark.

*On leave of absence.

There was never any flank pain with radiation to the groin. During the illness she had lost 6 pounds.

The family and past histories were noncontributory. The menarche occurred at fourteen and a half years. The cycle was regular at twenty-six to thirty days, and catamenia lasted four or five days without distress, except as already noted. There was no leukorrhea, and she denied venereal disease.

Physical examination disclosed a well-developed and well-nourished woman. A few small lymph nodes were felt in the left posterior cervical triangle. The heart and lungs were normal. There was no abdominal rigidity or tenderness. A firm, tender mass was felt in the left hypochondrium extending upward somewhat under the costal margin, laterally into the left flank, and downward and medially to the umbilicus. It seemed round, firm and smooth. It moved with respirations and slightly with change in position but had no notch. Fingers could be placed on the superior aspect of the mass, especially when the patient was lying on the right side.

The blood pressure was 138 systolic, 100 diastolic. The temperature was 98°F., the pulse 82, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,900,000, with a hemoglobin of 12.5 gm., and a white-cell count of 6700, with 73 per cent neutrophils, 15 per cent large lymphocytes, 9 per cent small lymphocytes, 2 per cent monocytes and 1 per cent eosinophils. A blood Hinton test was negative. The stools on three examinations were dark brown and guaiac negative.

A flat plate of the abdomen demonstrated a 7-cm., round, soft-tissue mass in the left midabdomen superimposed on the lower pole of the kidney. It showed central radiolucency. No unusual areas of calcification were seen, and an intravenous pyelogram was negative. The left ureter was incompletely filled in the region of the mass. During a barium enema, the barium passed through a normal rectum, colon and cecum. There was no connection between the bowel and the previously described mass.

An exploratory laparotomy was performed on the eighth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. THOMAS E. ANGLE: May we see the x-ray films?

DR. GEORGE W. HOLMES: There is only one obvious variation from the normal here, and that is the round mass which is described in the text. The colon was negative and in the lateral view the mass lies almost lateral to the vertebral

bodies, well back in the abdomen. The center of the mass is said to be translucent. That may be so, but I should not put much weight on that statement. If one could be sure of that observation I think the tumor would contain fat and would possibly be a dermoid cyst. But the colon overlies it, and the area of decreased density may be gas in the bowel rather than anything in the tumor itself. It would be interesting to determine whether the tumor was attached to the kidney and whether it moved with respiration.

DR ANGLEM: It did move with respiration. The matter of translucency bothered me a good bit.

DR. HOLMES: I should not disagree with that statement about radiolucency; however, I should not want to change my diagnosis on account of it.

DR ANGLEM: The onset of this patient's difficulty one month after delivery of a baby raises the question of whether or not this pregnancy was related to her subsequent difficulty. The only tumor that I can relate to pregnancy is chorion epithelioma, and the usual features of this disease are entirely lacking. It is safe to assume that the pregnancy was coincidental and had no bearing on the later troubles.

We are confronted, then, with a story of a mass in the left upper quadrant that had produced nausea, gradually increasing fatigability, increase in the patient's habitual constipation and a severe dorsal back pain, which was worse when she assumed the dorsal decubitus position and was relieved when she assumed a sitting posture; there was also one episode of crampy abdominal pain associated with catamenia. On examination a firm, round mass was found in the left upper quadrant, which was slightly tender, moved on respiration and had slight lateral mobility. The commonest mass in this location is an enlarged spleen. The physical characteristics of this tumor as described are not those of an enlarged spleen, which usually retains its general contour. I should think the physical findings were consistent with a tumor or cyst of the spleen, but I find it difficult to explain the other symptoms on this basis, and this holds true of the other intraperitoneal tumors that may occur in this area, such as mesenteric and omental cysts and tumors. Moreover, with a negative barium enema we have no evidence that this tumor originated in the large bowel, nor have we any convincing proof that the tumor originated in the small intestine. There is, however, considerable evidence in favor of a retroperitoneal position for this mass. The posterior reference of the pain, the increase in the pain on the assumption of the dorsal decubitus position, and the relief on assuming a sitting posture suggest to me a retroperitoneal mass with

stretching of the posterior peritoneum and stretching or irritation of the celiac plexus by the underlying tumor. The sitting position relaxes these structures. I believe the constant nausea may also be explained as a result of irritation or stretching of the celiac plexus.

The commonest solid retroperitoneal tumors that occur in this area are, first of all, those arising from retroperitoneal lymph nodes, namely, malignant lymphoma of any type. The mention of nodes in the posterior triangle of the left side of the neck suggests the possibility that this may have been a lymphomatous tumor with early generalization of the disease. However, lymph-node masses in the retroperitoneal area are almost invariably fixed and are not likely to show respiratory excursion or radiolucency. The other solid tumors that occur in this area are retroperitoneal lipoma and fibroma and a wide variety of less common tumors, such as those arising from the adrenal glands and rests and a large number of tumors of uncertain origin, some of which arise from fetal rests. Most of these tumors are fixed and unlikely to show respiratory excursions. Furthermore, they are unlikely to exhibit areas of radiolucency.

A wide variety of cystic tumors occur in this area, the commonest of which are the dermoid cysts. Unlike the solid tumors, the cystic ones are apt to show some degree of mobility, and it might be expected that such a cystic mass might show excursion on respiration. In addition to the dermoid cysts there are other cystic tumors, such as those arising from the mesentery of the large and the small bowel, the remains of the wolffian duct, and the lymphatic vessels. Rare cysts of enteric origin also occur, some of which are likely to be radiolucent in whole or in part. Cysts of the tail of the pancreas fulfill some of the requirements that we have to meet to explain this patient's symptoms. A cyst of the tail, unlike other cysts of the pancreas, may be relatively mobile and can show respiratory excursion, but again it is difficult to explain the radiolucency on this basis.

Lastly we have to consider tumors and cysts of the kidney. In spite of the fact that a pyelogram was negative and there was no evidence of intrinsic disturbance of the kidney, a tumor originating in the kidney capsule is entirely consistent with this picture. I refer to the mixed tumor of the kidney, which occasionally contains masses of fat and therefore might explain the central area of translucency. The absence of typical renal pain is a point against such an origin of this mass. However, it is possible for tumors of this type, particularly those originating in the kidney cap-

sule, to produce symptoms chiefly by pressure on and disturbance of contiguous structures without intrinsic disturbance of the kidney. The fact that the urine was not recorded interests me and suggests that something was found in the examination.

DR. TRACY B. MALLORY: It was entirely negative.

DR. ANGLEM: I believe that with tumors occurring in this area, particularly when the symptoms are as bizarre and unusual as those presented by

actually in the mesentery of the small intestine, then I cannot assume that. I think the possible explanation is that this was one of those bizarre enteric cysts with mucous cystic structures, which might contain any sort of filling, possibly necrotic cells that were responsible for the fat necrosis.

DR. MALLORY: How can one tie up this tumor with fat necrosis, Dr. Allen?

DR. ARTHUR W. ALLEN: This was a patient from my service on whom Dr. Robert Linton oper-



FIGURE 1. Photograph of Loop of Small Intestine, Showing Cyst in Mesentery (A) and Chalk-like Granules on Serosa (B).

this patient, it is almost impossible to make a precise diagnosis. All one can say with any degree of certainty is that the patient had a retroperitoneal tumor or cyst of unknown origin. I believe that the most likely diagnosis is mixed tumor of the kidney, with a central fatty area.

DR. MALLORY: Dr. Anglem has given an ingenious solution of this problem. I should like to show what the surgeon saw at operation and ask him to consider the matter further.

A large cystic mass was found in the mesentery of the small bowel, and over the adjoining loops of small bowel were little, bright-yellow, slightly chalky masses that grossly were characteristic of fat necrosis (Fig. 1). The opinion of the surgeon, as well as that of the consulting pathologist who was called to the operating room, was that it was a tumor in the mesentery, with thin chalky deposits characteristic of fat necrosis on the bowel and on the mesentery itself.

DR. ANGLEM: I am afraid that does not tell me very much except to suggest that the origin was in the tail of the pancreas. If this mass was

ated. The first operation consisted in looking at the cyst and removing one of these little nodules for biopsy. Rather at my insistence he reoperated a little while later and was able to remove this mass without damaging too much of the blood supply to the bowel. The question was whether it involved the mesenteric vessels so intimately that it could not be safely removed. It may comfort Dr. Anglem to know that we did not have any idea what this was until after the sections following the removal of the cyst were made.

CLINICAL DIAGNOSIS

Omental cyst.

DR. ANGLEM'S DIAGNOSIS

Retroperitoneal tumor or cyst (? mixed tumor of kidney).

ANATOMICAL DIAGNOSIS

Chylous cyst of mesentery of small intestine.

PATHOLOGICAL DISCUSSION

DR MALLORY: The answer to the problem is that the "fat necrosis" was not fat necrosis! All these little chalky spots consisted of dilated lymphatics filled with inspissated lipid material; adiposis of all lymphatics was present. The cyst itself contained putty-like grayish material. I think perhaps the radiologist's report of radiolucency was correct. There was nothing to indicate clearly whether this was neoplastic or entirely mechanical from beginning to end. I think it is quite possible that this was simply mechanical plugging of the lacteal system of the small bowel, with subsequent inspissation of fat from the local lymphatics. On the other hand, another possibility is that this was a lymphangiomatous cyst, which, in turn, had caused the lymphatic obstruction. There was no characteristic lesion that we could make out.

DR ALLEN: But you thought it was probably a chylous cyst at the time?

DR MALLORY: I still think so, but that does not prove whether or not it was of neoplastic origin.

DR ALLEN: A chylous cyst in the mesentery has been described. Was there any recognizable epithelial structure?

DR MALLORY: None whatever.

CASE 29272

PRESENTATION OF CASE

A thirty-seven-year-old man, a jewelry worker, entered the hospital complaining of chills, fever, abdominal pain and jaundice.

Eleven days before entry, after eating a heavy meal, he developed vague, abdominal discomfort. The following day he vomited, and two days later developed pain to the left of the umbilicus, which was relieved by an enema. During the next two days he had almost a constant urge to move his bowels but was able to pass only gas and a little fecal material. During the five days before entry he developed pain to the right of the umbilicus. The pain was cramplike, sharp, occurred at frequent intervals and did not radiate. Six days prior to entry he became jaundiced and his stools became clay colored. Two days later, however, the stools were yellow. During the four days prior to entry, the patient had chills and fever up to 103°F.

The family and past histories were noncontributory.

Physical examination showed a well developed and well nourished jaundiced man. There was dullness with absent breath sounds at both bases posteriorly. The abdomen was slightly distended, with moderate tenderness under the right costal

margin and in the right lower quadrant. There was no spasm. Rectal examination showed large hemorrhoids.

The blood pressure was 140 systolic, 80 diastolic. The temperature was 103.5°F, the pulse 140, and the respirations 40.

Examination of the blood showed a hemoglobin of 12.4 gm per 100 cc and a white cell count of 20,100, with 87 per cent neutrophils. The urine was dark amber in color and gave a ++ test for albumin and a ++ test for bile. The serum bilirubin was 4.1 mg per 100 cc, direct and 5.5 mg, indirect. The prothrombin time was 34 seconds (normal, 22 seconds). The hematocrit was 46.8 per cent. A blood Hinton test was negative. The stools were brown but bile negative.

A portable film of the chest showed a slightly elevated diaphragm on both sides and some atelectasis in the right lower lung field. A film of the abdomen showed a moderate amount of gas in the colon and stomach, but no definitely dilated loops.

For the first three days the fever ranged between 101 and 102°F, and the jaundice remained about the same. The liver was felt below the costal margin, but the abdomen remained unchanged. On the fourth day the abdomen was softer and there was no tenderness or spasm. The patient had some diarrhea; the stools continued to be brown but bile negative, and the urine to contain bile. Diarrhea continued for three days, and a proctoscopic examination showed two or three thrombosed hemorrhoids at the anal margin. The mucous membrane of the rectum appeared normal. Beginning on the fifth day the patient began to have a spiking temperature, ranging from 98 to 104°F each day. On the seventh day there were definite tenderness and resistance in the right upper quadrant, with a suggestion of a mass in this region. A serum bilirubin was 6 mg per 100 cc, direct, and 9 mg, indirect. A blood culture showed no growth. A Widal test was negative.

He was given vitamin K, transfusions and intravenous 5 per cent glucose in saline, but continued to run a spiking temperature with chills; he died on the sixteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR GORDON DONALDSON: In totaling up this patient's illness it is evident that he was sick for nearly a whole month before death. During the last twenty-two of these twenty-seven days he was jaundiced, and from the apparently acholic stools, the bile in the urine, the van den Bergh reactions and, finally, the appearance of a mass in the right upper quadrant, it is fair to say that he was suffer-

ing from an obstructive type of jaundice implicating the extrahepatic biliary system, rather than from a primarily portal type of cirrhosis. It seems unlikely that a diarrhea-producing toxin or chem-

to support the diagnosis of cancer of the bowel with metastases to the periportal lymph nodes or even to the liver itself. The onset of symptoms was much too fulminating and severe, and on entry



FIGURE 1. *Photograph of Liver, Showing Pylephlebitis and Multiple Abscesses.*

The arrow points to a thrombus in main portal vein.

ical could have so completely and suddenly eliminated bile secretion. So we shall say that he did have an extrahepatic biliary block.

There are, however, features in this story that direct attention to the remainder of the abdomen. The onset of pain was to the left of the umbilicus. Later it settled in the right abdomen, still at umbilical level. Moreover, the patient suffered recurrent diarrhea and occasional rectal tenesmus. Certainly the bowel itself was involved in this process. Typhoid fever can be ruled out by the white-cell count and the solitary negative Widal test. There are no stool cultures or examinations to lead us to implicate the other bacillary and amebic dysenteries. Any of these might have resulted in a primary dehydrating diarrhea and a later liver abscess, which obstructed the flow of bile and produced jaundice. Proctoscopy at such an early stage in the disease need not be positive, but in this case the negative findings probably help to rule out dysentery as a probable diagnosis. *Ascaris* infection, echinococcal disease and Weil's disease should be mentioned in passing as rare but unlikely possibilities. Likewise there is little

the patient is described as a young man in a state of good nutrition.

Subacute gallstone ileus could fit the bowel picture well. The passage of a foreign body through the small bowel would stimulate diarrhea and allow for a shift of the pain about the umbilicus. Moreover, it is described as cramplike, sharp and occurring at regular intervals, which is perfectly consistent with an obstructive, peristaltic type of pain, with the obstruction finally lodging in the terminal ileum. The abdominal film is of no help as no stones were seen, and any small-bowel dilatation would have been minimal in this type of obstruction. A spot x-ray film centered over the gall bladder might have been of real value in revealing stones. Certainly the events in the right upper quadrant were perfectly consistent with common-duct obstruction, perhaps caused by a second gallstone.

It is a little distressing to find that, in spite of all his fever and leukocytosis, there was never any striking tenderness or spasm in the right upper quadrant, at least until shortly before death. However, a deep-seated, thickened, sclerosed gall

bladder might still be inflamed and give little surface indication of its status. It is not uncommon for such an acute or subacute gall bladder by its very juxtaposition to the colon to give diarrhea

tion and jaundice. Acute cholecystitis itself may have caused common duct obstruction, but one would not expect the process to have been complete. The resulting cholangitis persisted. Mean-



FIGURE 2 Roentgenogram of the Upper Abdomen after the Injection of Thorotrast

Note the areas of decreased density (black) representing abscesses in the enlarged liver which has elsewhere taken up the Thorotrast to produce increased density (white). The spleen (arrows) which has uniformly taken up the Thorotrast is homogeneously dense.

and even tenesmus. The degree of bowel symptoms as given in the case history is certainly extreme. As for the locus of pain, it has been said that the gall bladder can give pain anywhere in the abdomen oftener and more atypically than any other organ.

The degree of cholangitis must have been marked, consistent with a complete mechanical biliary obstruction. The severe chills, spiking temperature and white cell count of 20,100 are to be expected in inflammation of the bile ducts. The early abnormal prothrombin time is perhaps more prolonged than one would expect in such an acute process, but still entirely possible.

The initial episode of vague abdominal discomfort followed by vomiting probably marked the onset of inflammation in the gall bladder. Irritation of the colon followed. A stone, which may have been passed at that time or may have already been in the common duct, caused obstruc-

tion and jaundice. Acute cholecystitis itself may have caused common duct obstruction, but one would not expect the process to have been complete. The resulting cholangitis persisted. Mean-

while other stones obstructed the bladder, aggravating the inflammatory process and leading to a palpable acute gall bladder or, more likely, to a palpable pericholecystic abscess. Probably at no time was the patient considered to be in good enough shape to allow surgical drainage, and he finally died of his infection and liver failure.

DR DWIGHT L. SISCOE. When one knows all the facts it is difficult to discuss the case without bias. Dr Donaldson has analyzed this patient's illness extremely well, especially the latter part of it. He would have achieved even greater accuracy if he had given more consideration to the onset of the illness, although the protocol perhaps does not emphasize some of the facts that stand out in my memory.

When I first saw the patient, three days after admission, I was impressed by the fact that he was a perfectly well, thirty-seven-year-old man, without antecedent history suggestive of disease,

who, a few hours after eating a large meal, developed nausea and vomiting followed in three or four hours by severe pain in the region of the splenic flexure, diarrhea and fever. This was associated with a constant urge to defecate and was relieved by an enema. Later,—we are told five days before entry, but it was actually twenty-four hours later,—he developed pain to the right of the umbilicus. This pain was constant and sharp, occurred at frequent intervals and did not radiate. Jaundice was not noted until six days after the onset. As Dr. Donaldson stated, these facts certainly implicate the intestines, and this is just the point that I think should be emphasized. It seemed to me that this was typical appendicitis, and we must not allow ourselves to be led astray by the fact that the original pain was on the left side of the abdomen. Diverticulitis and ulcerative colitis were considered and were the reason for proctoscopy.

DR. RICHARD H. SWEET: When I saw this patient he was quite ill, febrile and jaundiced, with a palpable slightly tender liver. There was generalized distention of the abdomen, but no signs of peritonitis. It was obvious from the clinical standpoint that he had pylephlebitis of the liver, but by that time there remained no localized signs of the original inflammatory focus from which it arose. All we had to go on were the history and the observations of the family doctor, who is an excellent observer. The latter reported that the tenderness and pain had been confined to the left lower quadrant. Because of that, although acute appendicitis is by far the most frequent source, I made the suggestion that the point of origin might have been a diverticulitis of the sigmoid.

CLINICAL DIAGNOSES

Appendiceal abscess?
Diverticulitis?
Pylephlebitis.

DR. DONALDSON'S DIAGNOSES.

Subacute cholecystitis.
Choledocholithiasis.
Cholangitis, intrahepatic.

ANATOMICAL DIAGNOSES

Appendiceal abscess.
Pylephlebitis.
Multiple liver abscesses.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The post-mortem examination revealed that the primary infection was in the appendix, which formed the base of a large abscess about 9 cm. in diameter. The appendiceal vein could not be identified, but the ileocolic vein was filled with pus and the phlegmon had extended into the portal vein, resulting in widespread intrahepatic pylephlebitis with multiple liver abscesses (Fig. 1). Although the bladder did have a few small stones and mildly inflamed there was no cholangitis and certainly was not a factor in the pathogenesis of the pylephlebitis.

The widespread distribution of the liver abscesses had been determined before death by intravenous injection of Thorotrast (Fig. 2), which proved that surgical drainage would have been futile. Occasionally, when there is one large abscess or one cluster of small abscesses, drainage may be attempted.

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JAUNDICE FROM HUMAN SERUM

EVER since immunization against yellow fever has been undertaken on a large scale there have been reports of jaundice of varying severity occurring in inoculated persons. In the early reports attempts were made to explain the occurrence of such cases on the basis either of coexisting epidemics of catarrhal jaundice or of actual infections with living yellow fever virus contained in the vaccine. These explanations have since been discarded as not entirely fitting the facts.

In 1939 about 1,300,000 persons received protective inoculations against yellow fever. One hundred and eighty seven different lots of vaccine were

involved, but in each the virus had been preserved in human serum. One lot alone gave rise to jaundice in 304 persons, or slightly more than one fourth of those to whom it was given. A change made in the seed virus seemed to eliminate the difficulty, but in 1940 many cases again appeared following the use of other lots of vaccine.

With the mobilization of troops for service in yellow-fever areas, vaccination against this disease was undertaken on a large scale among the armed forces, and during the first six months of 1942 over 25,000 cases of jaundice appeared among American troops who had received such protective immunization. There were 62 deaths, making a case fatality rate of about 0.25 per cent. The vaccine used in all these cases likewise contained human serum as a base.

More recently a change to a vaccine with an aqueous base seems to have eliminated this complication, without impairment of the immunizing qualities of the vaccine, as indicated by laboratory tests. Over six hundred thousand doses of this aqueous base vaccine prepared by the United States Public Health Service have now been used, and no untoward effects have been recorded after an apparently adequate period of observation.¹

In Great Britain, cases have been encountered in which jaundice and the other symptoms characteristic of the syndrome following the inoculation of yellow fever vaccine occurred after the injection of human serums that did not contain yellow-fever virus. Medical officers of the British Ministry of Health have recently prepared a thought provoking review of the present knowledge and recent experiences in this field, under the title "Homologous Serum Jaundice." A few of the outbreaks noted in this report, other than those following yellow-fever vaccine, deserve brief mention.

The earliest cases date back to 1885, when 191 cases of jaundice occurred in Bremen several weeks after vaccination of 1289 shipyard workers with a "glycerinated humanized lymph." In two groups of workers in the same shipyard who were vaccinated at the same time with different batches of lymph, no jaundice occurred.

In 1937, an outbreak occurred in which 41 out of 109 recipients of a single batch of measles convalescent serum given subcutaneously developed jaundice, and 8 of them died. These cases were scattered through the southern part of England. In addition, 11 cases of jaundice were reported following the injection of pooled Berkefeld-filtered measles adult serum, with 1 death.

In March, 1942, of 266 British troops who each received less than 14 cc. of Seitz-filtered mumps convalescent plasma in one or two doses intravenously, 86 developed jaundice. Furthermore, 48 cases of jaundice following the injection of mumps convalescent serum were studied at the Harvard-Red Cross Hospital.

In Great Britain, about a dozen cases have also been reported in which jaundice occurred after a long interval following the last of a series of transfusions of large amounts of dried and reconstituted human serum. And, cases following repeated whole-blood transfusions have been noted.

In this country, Beeson³ has reported 7 cases of jaundice that occurred from one to four months after transfusions of blood or plasma given at the time of injuries or of surgical operations. Three of these cases were recent, and 4 were culled from the records of 79 cases at the Grady Hospital in Atlanta in which the patients had been diagnosed as suffering from acute catarrhal jaundice or toxic hepatitis. Clinically these cases were similar to the mild cases of jaundice in the groups already mentioned.

Jaundice was the outstanding clinical feature in all these cases, and varied in severity. In the fatal cases, there was a fulminating hepatic necrosis, and widespread changes in other organs. Splenic enlargement was inconstant. Urticarial and other rashes, usually classed as erythema multiforme, occurred in almost half the cases. Stiff joints without swelling occurred in about one fourth of them. There was some itching before the onset of jaundice. Anorexia, nausea and a heavy feeling in the epigastrium were the other frequent symptoms. The latent period between injection and symptoms

was usually between sixty and ninety days, ranged from two to eighty weeks.

Analogous conditions have apparently been countered in horses after the injection of homologous immune serums prepared in other horses but not with serums prepared in other animals; hence the designation "homologous serum jaundice."

In the cases of jaundice in human beings, factors in the serum responsible for this condition have not yet been identified. Data concerning donors are difficult to obtain in retrospect, and records are incomplete. Furthermore, the incidence and the occurrence of this complication are difficult to determine because of the long incubation period. This makes it highly essential to keep complete records concerning the donors and recipients of all preparations made from human blood. In the past it has been necessary to inquire concerning drugs and other toxic agents in all cases that might be classed as catarrhal jaundice or toxic hepatitis. Now it is also necessary to consider previous inoculations as a possible cause of the jaundice in such cases. Only in this way can we hope to obtain further information regarding this extremely interesting and baffling condition that may be useful both in its prevention and in its management.

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NEW TREATMENT FOR THE "HOOPING COUGH"

WILLIAM Moss, of Liverpool, writing about 1784 in *The Liverpool Guide*, made the following shrewd remarks concerning the treatment of the chin-cough, known variously as "hooping cough," "whooping cough" and plain "pertussis": "When the complaint takes a favorable turn it is frequently attributed to the means that were last used: hence that means is ever after recorded as infallible. As

it is a disease of the spasmodic or convulsive kind it has been sometimes relieved, or even removed, by a shock or sudden fright: thus riding upon a bear (a frightful mode of travelling no doubt) from the fright it occasions has been said to be serviceable. Giving the patient a part of some disgusting animal, as a mouse, &c., to eat, and afterwards informing him of it; and so forth."

The diversity of the methods of treating whooping cough offers the best evidence of the intractability of the infection and the uncertainty of its course. The drugs that have been used for its alleviation are legion: garlic has been put in the shoes of its victims; they have been taken to the gas works to inhale the invigorating chlorine fumes, they have been treated by x rays, have been injected with serums, vaccines and undenatured bacterial antigens and have received topical applications to the upper reaches of the nasal mucosa. To Osler has been attributed the one form of therapy that has been proof against time—six weeks and a good big bottle of paregoric.

Practically every form of treatment that has been used has been apparently effective in a sufficient number of cases to attract a certain number of adherents, for even whooping cough must some time come to its conclusion; any sedative form of treatment is certain to be palliative to some degree, although none can claim consistently spectacular results. The Sauer type of vaccine given in large doses can be considered as prophylactically successful.

The December 26, 1942, issue of the *British Medical Journal* makes editorial comment, under the title "High Flying for Whoopers," on one of the newer and more novel forms of treatment, as developed and published by the Berne school of medical practice. By this method of treatment, whoopers in scientifically impressive numbers were given ninety minute airplane flights, ascending not too rapidly to an altitude of eleven to twelve thousand feet, which was maintained for forty minutes. An abrupt cure was registered for 22.8 per cent, with another 32 per cent cured within eight days. A

second flight was sometimes necessary. Less spectacular, the Jungfrau was ascended by rail by another group, with no benefit accruing. Truly impressive results, however, were obtained by placing patients in a low pressure chamber for thirty minutes, there being 31 per cent of immediate cures, with an additional 50 per cent improved.

If these results can be consistently obtained something of real value has been offered—provided enough low-pressure chambers can be made available when the need for them arises.

MEDICAL EPONYM

WILLIAMS'S TRACHEAL TONE

This physical sign was described by Dr Charles J. B. Williams (1805-1889) in the fifteenth of a series of lectures delivered to the students of St. George's Hospital, London, during 1836 and 1837. The lectures were published in the *London Medical Gazette* and in book form, both in London and Philadelphia, in 1838 and 1839. The following is a quotation from page 148 of *Lectures on the Physiology and Diseases of the Chest* (Philadelphia, 1839):

in dilated bronchi, if any dulness exist, it is generally in the mammary, lateral or scapular regions of the chest, and is often accompanied by a sound of a peculiar kind. This is a hollow tube like sound, and from its semblance to that produced by mediate percussion on the trachea, or by tapping with the finger on the mouth of a small phial, I have given it the name of *tracheal* or *amphoric*. I can give you a notion of the kind of sound, by filling up a finger pressed on the larynx or trachea, or on the cheek when the mouth is opened in the manner of sounding the letter O.

In the sixteenth lecture, page 161, Dr Williams mentions the occurrence of the same sound in certain cases above the dullness due to pleural effusion.

Let this portion of lung be perfectly condensed by a liquid effusion, or perfectly consolidated by hepatization, and you will then get the bottle note of the tubes, just as you do of the windpipe where no lung intervenes. But since my attention has been drawn to it, I have met with several cases of both pleurisy and pneumonia in which it existed in a smaller degree, and I had occasion to notice in the last lecture that it sometimes occurs with dilated bronchi.

R. W. B.

ficer it should be of equally great value to the industrial and orthopedic surgeon engaged in civil practice.

The manual is divided into four major sections: united fractures; injuries of the spinal column; compound fractures; and osteomyelitis. The text is well written, and the procedures advocated are clearly described. Adequate warning is given of complications and of the dangers to be avoided. Whereas undue emphasis is given at times to the favorite method of treatment of the surgeon who has written each chapter, the general directions are sound and are stated in a simple understandable manner.

This is an excellent manual, well conceived and ably written. Although it will not make orthopedic surgeons of the medical officers who first treat these injuries, it should lead to greatly improved care, to a rapid return of function and to a great decrease in permanent disability.

First Aid and Bandaging. By Arthur D. Belilios, M.B., B.S. (Lond.), D.P.H. (Eng.), and others. 16°, cloth, 628 pp., with 239 illustrations. Baltimore: The Williams and Wilkins Company, 1942. \$1.75.

This handbook gives a comprehensive exposition of its subject, from the general principles of first aid through all the special sections that are necessary in any consideration of this subject. It even takes up the subject of first aid in maternity cases. The section on the treatment of hemorrhage is clearly and soundly given so that a first-aid student can easily grasp the situation.

The three chapters on the respiratory system, resuscitation and asphyxia are well illustrated and much to the point. In the section on burns, the question of shock and excluding air from the burned surface, the removal of clothing and absolute cleanliness are given the importance that they deserve. As in so many first-aid books, immediate treatment with a solution of sodium bicarbonate is given prominence. It is of interest to read that the well-known, earlier treatments with carron oil and with various ointments are only mentioned as having now been discarded, at least in all but the most trivial burns. The triple-dye treatment is given prominence.

The following apt quotation is taken from the first section of the book: "First aid cannot be learned entirely from a textbook, nor can it be practiced by rule of thumb. The layman who attempts to do without professional assistance is not practicing true first aid." Certainly the student of first aid will learn from this book that overzealousness may result in harm to the patient in attempting too much too quickly.

Shock: Its dynamics, occurrence and management. By Virgil H. Moon, M.Sc., M.D. 8°, cloth, 324 pp., with 36 illustrations. Philadelphia: Lea and Febiger, 1942. \$4.50.

The basis for this text may be stated briefly as follows: Shock results from leakage through capillary walls, not only at sites of injury but throughout the body, particularly in the viscera. The resulting decrease in effective circulating plasma volume causes tissue anoxia and therefore death. If there is no local trauma, capillary leakage is assumed to result from various deleterious agents affecting the capillary walls directly or as a result of the anoxia caused by such agents. The evidence for capillary leakage is the presence of congestion of the peripheral vessels, petechial hemorrhages, edema and effusions, which are uniformly present in all types of shock. Since hemoconcentration is an inevitable sequel, it is always present.

Such phenomena will not be found in hemorrhage, because hemorrhage is not shock.

The data are woven into a pattern that results in a reaffirmation of the classic view of shock. The author, however, has found it desirable to redefine shock as follows: "Shock is a disorder of fluid balance resulting in a peripheral circulatory deficiency which is manifested by a decreased volume of blood, reduced volume flow, hemoconcentration, and by renal functional deficiency." No doubt this definition will require alteration in the light of the enormous mass of new data that are now being gathered. For example, there is recent evidence contradicting the theory of leakage through capillaries outside local areas of injury. The kidney, furthermore, although a vital organ, is no more important than the liver, the function of which has also been shown to fail.

The reviewer believes that much of the evidence cited in support of the author's viewpoint is too selective, and some of it insufficient in detail, to be convincing. The case histories in support of the evidence for hemoconcentration (pp. 249-251) are an illustration in point. So far as the pathological data on leakage are concerned, the presence of congestion and petechial hemorrhages does not necessarily imply the existence of increased capillary permeability.

A number of statements are of dubious validity. Examples of such statements are the following: Page 24—"[Among the clinical signs of shock] there is a constant thirst but efforts to relieve it are ineffectual because of persistent vomiting. . . . Often there is diarrhea. . . ." Page 50—"If arterial vasoconstriction were an important primary factor initiating shock, one would expect that syndrome to develop occasionally in cases of so-called essential hypertension. . . . An extensive superficial burn will result in shock in a degree proportional to the severity and the area of the burn. If treated promptly, as with tannic acid, shock may not develop or will be of lesser degree." Page 126—"In one group of experiments, a neutralized solution of trypan blue, pH 7.6, was injected intravenously when examinations of the blood indicated that hemoconcentration was developing. Extensive visceral areas were found at necropsy to be stained with the dye. . . . Likewise the serous effusions in the pleural and pericardial cavities were distinctly tinged with blue. The muscles and other peripheral tissues were not affected. *These results indicate that capillary endothelium in extensive visceral areas became abnormally permeable to colloids. The permeability and the loss of fluid were not limited to the area of tissue injury. This finding is incompatible with the belief that shock is due to loss of fluid in local areas of trauma.*"

In the reviewer's opinion, the book is not likely to rank among the enduring contributions to the subject of shock.

A Textbook of Clinical Neurology, with an Introduction to the History of Neurology. By Israel S. Wechsler, M.D. Fifth edition. 8°, cloth, 840 pp., with 162 illustrations. Philadelphia and London: W. B. Saunders Company, 1943. \$7.50.

Four editions of this popular textbook have been called for since it was originally issued in 1927. Since the last edition, four years ago, new material has been added regarding chemotherapy, headache, electroencephalography and a few other topics. The book is therefore improved and its usefulness enhanced.

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THIOURACIL IN THE TREATMENT OF THYROTOXICOSIS*

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A FEW cases of thyrotoxicosis must of necessity be treated by nonsurgical methods, and in some other cases such methods are preferable. Whether one can expect to treat most of the cases effectively by medical means is only conjectural, since the etiology of thyrotoxicosis and all the entities involved in its production are obscure. Thus far, the measures employed in the medical treatment of this condition, although quite effective in some cases, do not work out satisfactorily in the majority. Moreover, it is not known why iodine is effective in some cases and not in others, and its mechanism of action is uncertain. Such a state of ignorance induces one to approach the matter from various angles.

During the last few decades quite a large number of goitrogenous agents have been described. The effect of many of these substances has been attributed to the alterations in the iodine metabolism that they induce, since the simultaneous administration of iodine inhibits the goitrogenous effect. Certain other substances, such as cyanide, presumably induce goiters by inhibiting the biologic oxidation of the body cells. However, there have recently been described^{1,2} certain substances that induce goiter, presumably by their direct action on the thyroid gland. These are the sulfonamides, thiourea and thiourea derivatives. Following their administration to certain animals, particularly rats, thyroid enlargement results in a few days. Histologically, one finds hyperplasia of the acinar cells and a decrease in the colloid of the follicles. A drop in the basal metabolic rate occurs, and after a few weeks may be marked. These changes can be prevented by the administration of desiccated thyroid or thyroxine. They can also be prevented by

hypophysectomy but not by the administration of iodine. In rats fed sulfaguanidine changes in the pituitary glands similar to those following thyroidectomy take place. These facts suggest that the above drugs act directly on the thyroid gland, inhibiting the production of thyroxine, thus in turn leading to a decrease in the body metabolism and to an increased activity of the pituitary gland.

Astwood³ tested the goitrogenous effect of a large number of sulfonamides and derivatives of thiourea. He found 2-thiouracil to be the most active substance tested. He used this substance in the treatment of 3 patients with thyrotoxicosis and found that it lowered the basal metabolic rate and caused a remission of symptoms, but when used for only a month a relapse followed its discontinuance. One of his patients, while receiving 2 gm. of thiouracil daily, developed agranulocytosis. Several patients with nonthyroid conditions treated with thiouracil experienced no drop in the basal metabolic rate.

During the last few months we have been studying some of the pharmacologic and therapeutic effects of thiouracil.[§] In this paper we are considering its effect in the treatment of patients with thyrotoxicosis. We have treated all the patients with this disease whom we could find. All patients treated are included in this report. The case reports are given below, comment on them being confined chiefly to the factors that relate closely to the thyroid gland. In addition to the treatment with thiouracil we have given much attention to the patient's general condition. In most cases we prescribed supplemental amounts of thiamine, niacin, civitamic acid and yeast. Several patients with menopausal symptoms were treated with diethylstilbestrol. All the patients were given sedatives at night. None of them were confined to bed. None of the patients were given iodine, with the exception of one who had siphilitic laryngitis, and in this case the iodine treat-

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§The thiouracil was supplied by the Lederle Laboratories Incorporated, Pearl River, New York.

ment was not begun until after the basal metabolic rate had reached a minus level. All the thiouracil was given by mouth, usually in doses of 0.2 gm.

CASE REPORTS

CASE 1. V.S. (No. 1950T), a 27-year-old man, was admitted to the hospital on January 14, 1943, chiefly be-

There was a fine tremor of the fingers, tongue and eyelids. The pulse rate was 115 and the blood pressure was 140/70. The heart sounds were loud. A slight gynecomastia was present bilaterally.

On February 18, the basal metabolic rate was +66 per cent and the weight was 143 pounds. The protein-bound iodine of the plasma was greatly elevated (28 microgram per 100 cc.—normal, 4 to 8 microgm). Treatment with

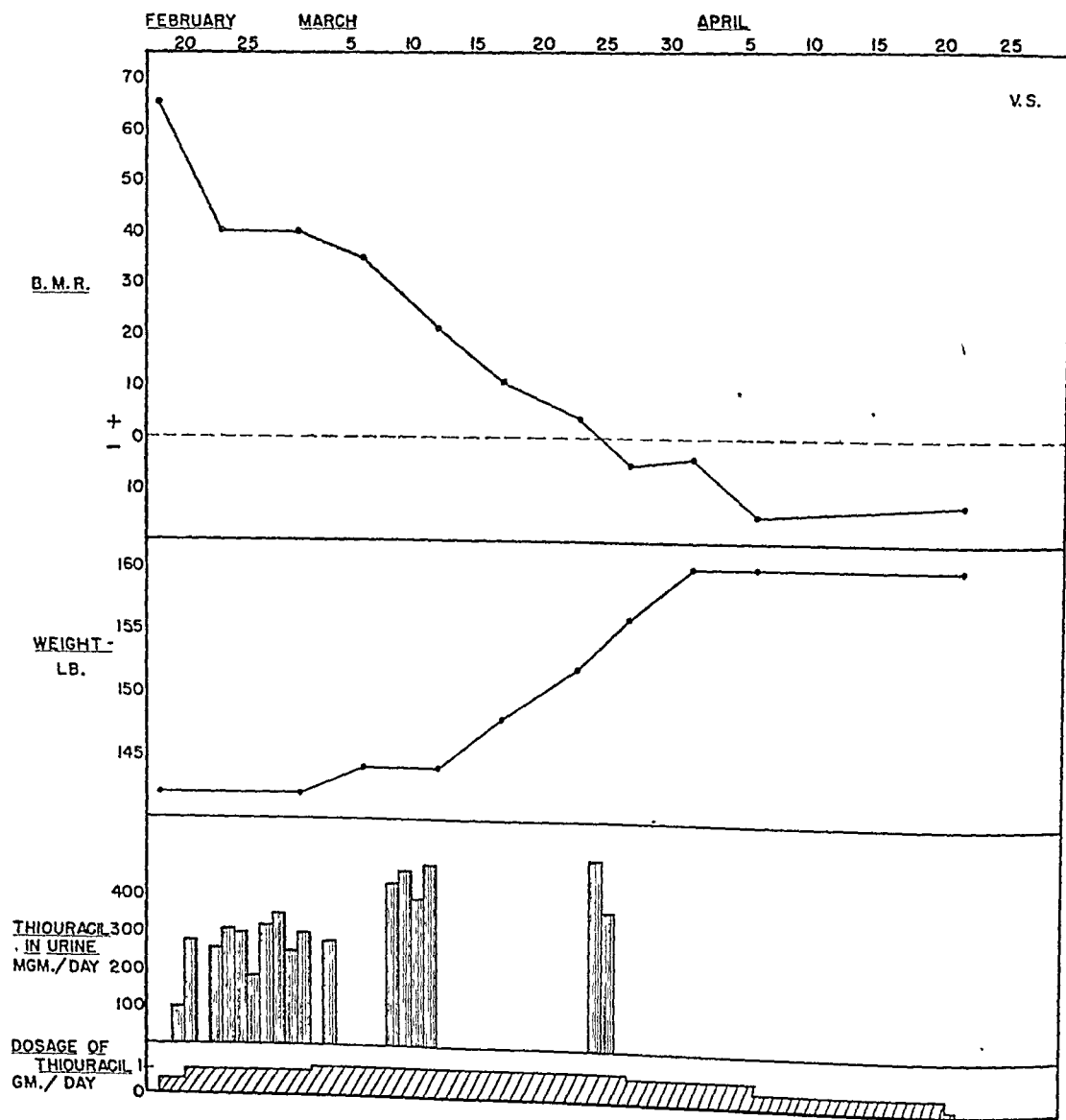


FIGURE 1. Case 1.

Note the rate of excretion of the drug in the urine.

cause of acute pharyngitis and laryngitis, which were treated with sulfadiazine. During the previous 6 months he had lost 40 pounds in weight, had become restless and nervous, and complained of intolerance of hot weather. Diarrhea was not infrequently present. He had also been bothered with palpitation and exertional dyspnea.

On physical examination the patient was apprehensive, restless and excitable. The skin was hot, moist, fine and smooth. No eye signs were present. The thyroid gland was enlarged diffusely to three times its normal size; it was firm and smooth, and a bruit was heard.

thiouracil was started, the dosage being 0.2 gm. three times daily. After 2 days this was increased to 0.2 gm five times daily. Within a few days there was a distinct clinical improvement and the metabolic rate began to fall (Fig. 1). On March 2, the dosage of thiouracil was increased to 0.2 gm. every 4 hours. By March 23, or 5 weeks from the initiation of the thiouracil treatment, the metabolic rate had returned to normal (+3 per cent). The dosage of thiouracil was gradually reduced to 0.2 gm once daily. This dosage has been satisfactory in maintaining the metabolic rate at a normal level.

Associated with the drop in the metabolic rate there was a clinical response of equal degree. All the symptoms of thyrotoxicity disappeared. A definite effect was noticeable a few days after the treatment was started, but the most rapid response was from the 3rd to the 5th

CASE 2. F.D. (No. 1098272), a 55-year-old painter, was admitted on February 27, 1943. The onset of thyrotoxic symptoms occurred 2 years before seeking treatment. The patient lost 24 pounds in weight, became nervous, perspired excessively and was troubled with

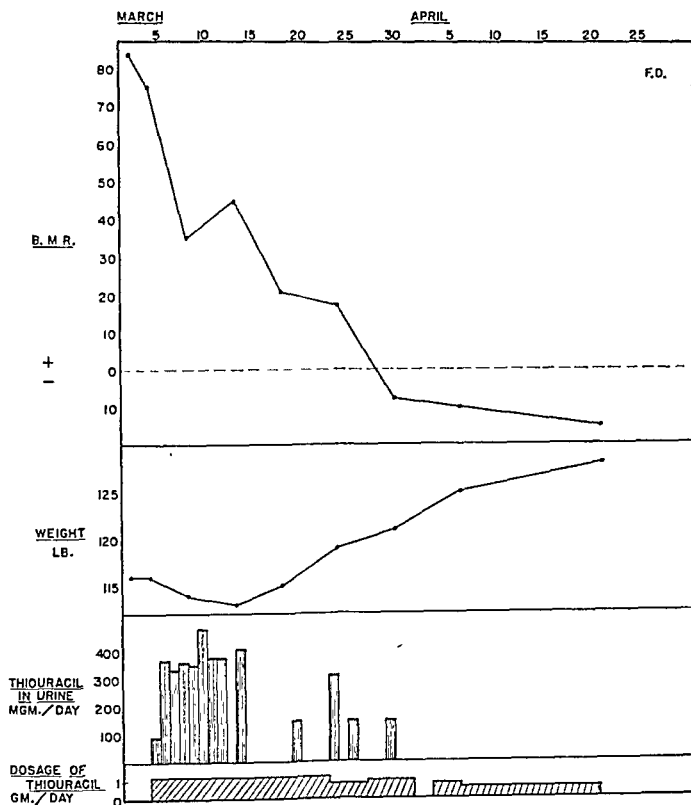


FIGURE 2. Case 2.

Note the amount of the drug excreted in the urine.

week. The patient gained 15 pounds in weight within 3 weeks. On May 15, the protein-bound iodine of the plasma was 5.1 microgm. per 100 cc.

During the first few days of treatment there was an increase in the consistence and size of the thyroid gland. Thereafter it became softer than at any time previously and decreased in size, although it was still above normal size. No eye signs of Graves's disease developed.

While the patient was receiving 1 gm. of thiouracil daily he excreted about 300 mg. in the urine per day. When the dosage was 1.2 gm., he excreted about 400 mg. per day. Stool specimens saved for a period of 4 days contained no thiouracil.

The patient was kept in the hospital for 6 weeks. Three weeks after discharge he was permitted to resume his work.

palpitation and dyspnea. Only slight prominence of the eyes had been noticed.

On physical examination the patient was restless and excitable. The skin was hot, fine and sweaty. A marked tremor of the hands was present. There was slight exophthalmos—each eye measuring 18 mm.—with widening of the palpebral fissures, conjunctival injection, palpebral edema, slight chemosis and lacrimation. The thyroid gland was about three times normal size, firm and slightly nodular. There was slight cardiac enlargement. The pulse was grossly irregular in force and rhythm, having an apical rate of 170 and a radial rate of 110. The blood pressure was 130/70.

On March 2, the basal metabolic rate was +84 per cent, and 2 days later it was +74. On March 4, the patient began receiving 0.2 gm. of thiouracil every 4 hours.

He excreted about 350 mg. of this drug per day in the urine. The metabolic rate fell rapidly, reaching a normal rate (-7 per cent) in less than 4 weeks from the beginning of treatment (Fig. 2). On April 7, the protein-bound iodine of the plasma was 1.8 microgm. per 100 cc., which is definitely in the myxedematous range.

Concomitant with the changes in the metabolic rate there occurred a marked clinical improvement. All the symptoms of toxicity disappeared and the patient gained 12 pounds in weight. The auricular fibrillation ceased spontaneously early in the course of treatment. It reappeared but was stopped with quinidine and did not return. The thyroid gland became distinctly softer and somewhat smaller.

The condition of the patient's eyes was followed carefully because it was realized on the first examination that the changes in the eyes, although mild at the time, were of the type that leads to the classic state of so-called "malignant exophthalmos."⁴ After having received thiouracil for 2 weeks, the ocular disturbances became more marked. There was a slight increase in the exophthalmos (measurement, 20 mm.), the lacrimation, the palpebral edema and the chemosis of the conjunctiva. Previous experiences with a large number of patients with this ocular complication⁴ led us to conclude that desiccated thyroid is of advantage in the treatment of this condition. On April 9, after the basal metabolic rate had been maintained in a normal range for 10 days, the patient was given desiccated thyroid, 0.5 gr. per day. At the same time treatment for syphilis of the larynx was started. This consisted of weekly injections of 0.13 gm. of bismuth salicylate and 5 drops of a saturated solution of potassium iodide three times daily. The laryngitis improved rapidly, and there was no thyrotoxicity induced by the iodide, as occurred when Webster and Chesney⁵ gave this substance to rabbits with goiters induced by cabbage. The eyes showed definite improvement, but this was more pronounced when the dosage of thyroid was increased to 1 gr. per day on April 21.

On April 12, 2 days after discharge, there developed swelling and slight tenderness of the submaxillary salivary glands. However, these glands subsided in spite of continued treatment with thiouracil.

The metabolic rate has been normal for the last 6 weeks, and during this time there has been no clinical evidence of thyrotoxicity. The patient has continued taking thiouracil daily, but the dosage has gradually been reduced from 1.2 to 0.4 gm. He is now working regularly as a painter.

CASE 3. K.T. (No. 1099647), a 54-year-old woman, was admitted on March 11, 1943. Onset of thyrotoxic symptoms occurred 1 year before seeking treatment. The first manifestation was nervousness, leading to restlessness, insomnia, frequent crying spells and tremor of the hands. A short time later she began to lose weight, in spite of an increased appetite, having lost 22 pounds within a few weeks. She had no diarrhea. Her eyes developed a stare. She became sensitive to hot weather and perspired excessively. For 6 months she had experienced exertional dyspnea and swelling of the legs, the latter being more marked at night. For 3 months she had been treated by a physician for a toxic goiter, the treatment consisting of rest and large doses of sedatives, but no iodine.

On physical examination the patient was restless and emotionally unstable. The skin was hot, fine, moist and

red. There was a marked tremor of the hands, eyelids and tongue. The eyes had a distinct stare but there was no exophthalmos. The thyroid gland was diffusely enlarged, being about three times normal size. It was firm and smooth in outline, and a distinct bruit was heard. The pulse rate was 105. The blood pressure was 140/75. The heart sounds were rapid and forceful.

On March 12, the basal metabolic rate was $+80$ per cent and the weight was 126 pounds. The protein-bound iodine of the plasma was 21 microgm. per 100 cc. Immediately thereafter the patient began receiving 0.2 gm. of thiouracil every 4 hours. With this dosage she excreted 400 mg. of the drug per day in the urine (Fig. 3). However, stool specimens collected for 4 days contained no thiouracil.

Within $3\frac{1}{2}$ weeks after treatment with the drug was begun, the basal metabolic rate reached a normal range and has remained there during the subsequent 6 weeks that she has been followed. On April 12, the protein-bound iodine of the plasma fell to 5.7 microgm. per 100 cc. The clinical response has been in accord with the changes in the metabolic rate. The patient has gained 13 pounds in weight and all signs of thyrotoxicity have disappeared. The stare is no longer present and no other eye signs have developed. The thyroid gland increased slightly in size during the first few days of treatment. It then began to get smaller and softer, now being about twice normal size. A bruit is still present.

After having taken thiouracil for 3 weeks, in doses of 1.0 to 1.2 gm., the patient developed puffiness of the eyelids and definite edema of the legs. She had had edema of greater degree periodically during the preceding 6 months. On investigating the etiology of the edema no evidence of heart failure was found. The urine was negative; a phenolsulfonephthalein test was normal. The total serum protein was 7.38 gm. per 100 cc. and the nonprotein nitrogen 25 mg. However, the serum chloride was found to be 116 milliequiv. per liter. At the time that the edema appeared the basal metabolic rate was $+1$ per cent and the dosage of thiouracil was 0.2 gm. five times daily. This was reduced to 0.2 gm. three times daily, and within 3 days the edema disappeared and the serum chloride returned to normal, the metabolic rate remaining normal.

The patient was kept in the hospital for 1 month, had restricted activities for the next 2 weeks, and since then has carried out her usual program as a housewife. She is now taking 0.2 gm. of thiouracil per day.

CASE 4. R.L. (No. 1099980), a 49-year-old factory worker, was admitted on March 15, 1943. She had not been well since the first onset of thyrotoxic symptoms 22 years previously. At that time she had three operations for toxic goiter, and following the last operation was told by her surgeon that she should never be operated on again. She experienced a distinct improvement following these operations but never became free of toxic symptoms. The patient, as well as her relatives and friends, had noticed that she always tended to be overactive and restless. The eyes remained prominent and she had had a goiter throughout most of the 22 years. There was a progressive loss of weight and strength until the patient became emaciated. During the year before admission the symptoms of toxicity increased, with further enlargement of the goiter, more pronounced sweating, nervousness, palpitation and weakness. During the few months before hospitalization there was a hacking cough, dyspnea,

orthopnea and transient edema of the legs. She had taken digitalis intermittently during this time. Throughout the 22 years she had periodically taken Lugol's solution, with some improvement in symptoms.

Physical examination revealed a tall, weak, emaciated woman, who was restless, apprehensive and irritable. The

The patient had a great fear of having another thyroidectomy and for this reason was constantly begging to leave the hospital. She refused to consider medical treatment of her toxic goiter because the many years of such treatment had fully convinced her that the condition could not be improved. She detested hearing the

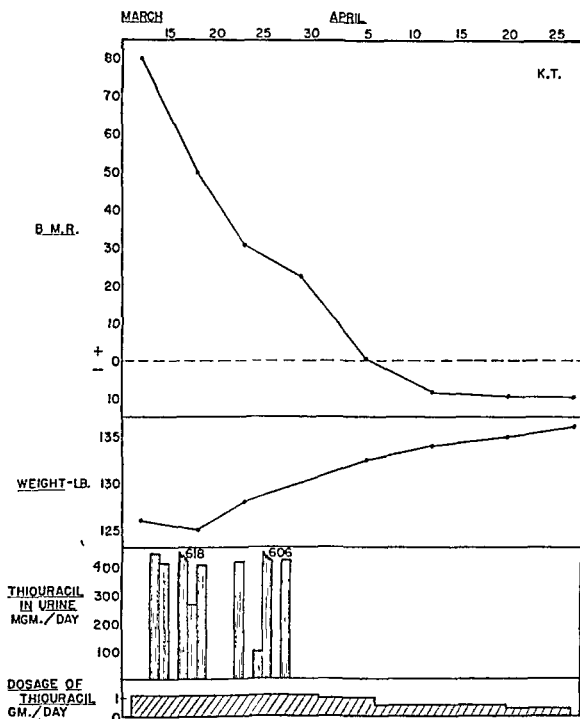


FIGURE 3. Case 3.

Note the rate of excretion of the drug in the urine.

skin was hot, moist, smooth, fine and somewhat loose. Over the elbows and heels it was fiery red, owing to restlessness in bed. The eyes truly had the appearance of pop eyes, there being a pronounced stare and wide palpebral fissures. The exophthalmos appeared marked, but measurement showed it to be slight (20 mm.). No palpebral edema was present. The tongue was bright red. The neck was long and slender. A goiter was readily visible above the old thyroidectomy scar. There was two to three times the normal amount of thyroid tissue. It was hard and slightly irregular in outline, and a bruit was heard. The pulse was grossly irregular in force and rhythm; its rate was 110. The blood pressure was 120/60. The heart was moderately enlarged and its contractions were forceful. No murmurs were heard. There was slight pitting edema of the legs, and a few varicose veins. A fine tremor of the fingers was present.

name "goiter" or anything pertaining thereto, because, as her sister stated, "it is like scraping an old and painful sore." The patient presented a good picture of a long-term thyrotoxicosis. Although weak and exhausted to the point of having to be supported in walking, she was begging to go back to work.

On March 16, the basal metabolic rate was +56 per cent. A few days later the patient began receiving 0.2 gm. of thiouracil four times daily. After 2 days, since she had not been upset by this medication, the dosage was increased to 0.2 gm. every 4 hours. On this dosage she excreted 250 mg. of the drug per day in her urine (Fig. 4). During the first 2 weeks of treatment she showed only slight improvement. The course was complicated by the development of several corneal ulcers in each eye owing to exposure during sleep. The diet was supplemented with niacin, thiamine, riboflavine, cevitamic

acid and vitamin A. However, the condition of the eyes and the slowness in gaining weight caused her to be somewhat discouraged. In an attempt to break a vicious cycle she was given 10 mg. of methyl testosterone three times daily for 5 days (we hesitated to use larger quantities of this drug since it sometimes causes elevation in

now been reduced to 0.2 gm. three times daily. The patient has been permitted to return to work.

CASE 5. M.R. (No. 1101316), a 35-year-old housewife, was admitted on March 12, 1943. She had been well until 1 year previously, when she became restless, irri-

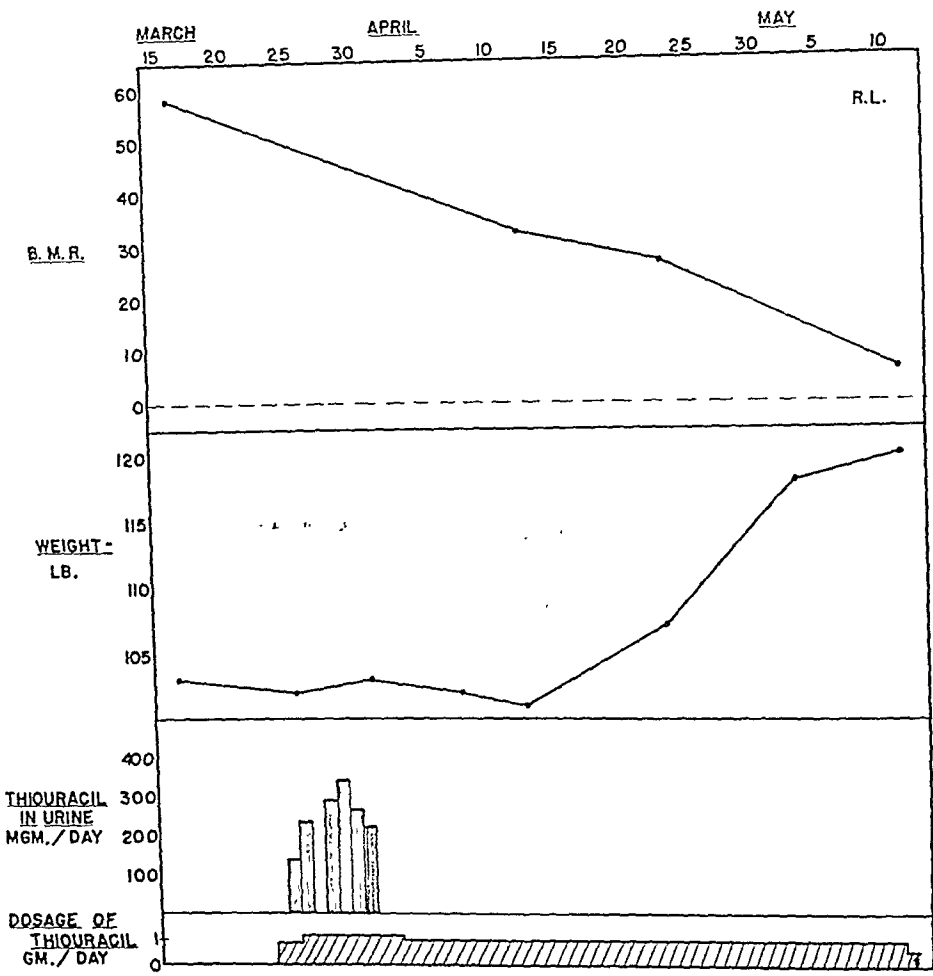


FIGURE 4. Case 4.
The infrequency of the metabolism tests was due to the patient's refusal to have them run.

the basal metabolic rate).⁶ The methyl testosterone appeared to have improved the patient's strength and mental attitude to a slight extent. After having received treatment with thiouracil for 3 weeks the patient left the hospital, against advice, but carried on her treatment faithfully at home. During the 4th week of this treatment she improved rapidly and continued to do so. By May 11 she had gained 16 pounds in weight and the thyrotoxic state had disappeared. The eyes showed a decrease in stare. The amount of thyroid tissue had not changed much, but the gland was not quite so firm as originally. A distinct improvement in the cardiac status had occurred, but the auricular fibrillation was still present.

The patient so disliked basal-metabolism tests that she would not permit many of them. However, the tests that were run showed essentially a straight-line drop from +58 to +7 per cent. The dosage of thiouracil, which for the most part had been 0.2 gm. five times daily, has

table, excitable and easily upset. Thereafter she experienced insomnia, heat intolerance, diarrhea, a loss of 20 pounds in body weight, slight exophthalmos, fullness in the neck, palpitation and exertional dyspnea. On physical examination the patient was restless, apprehensive and excitable. The skin was hot, moist and smooth and exhibited vitiligo on the dorsum of the hands. There was slight exophthalmos and a small amount of palpebral edema. The thyroid gland was two to three times normal size, slightly irregular in outline and firmer than normal. The pulse rate was 110 and the blood pressure 130/75. The heart sounds were forceful. On March 13, the basal metabolic rate was +45 per cent. On that date the patient began receiving 0.2 gm. of thiouracil five times daily, but only a few hours later left the hospital owing to her anxiety over her six children and her undependable husband. However, she continued the prescribed treatment at home, returning to the hospital at weekly intervals. The metabolic rate progressive-

ly declined reaching a normal level in 6 weeks (Fig 5). It remained normal during the subsequent 3 weeks. With in the same time the protein bound iodine of the plasma fell to a subnormal level (2.1 microgm per 100 cc). Throughout most of the period of treatment the dosage of the thiouracil was 1 gm daily, but it was gradually reduced to 0.4 gm daily after the metabolic rate had become normal. The clinical improvement exceeded the response in the metabolic rate. Before the latter had become nor-

The basal metabolic rate on April 20 was +88 per cent. The following day treatment with thiouracil was started, the dosage being 0.2 gm every 4 hours. Basal metabolic rates taken at weekly intervals were +55, +9, +18 and +5 per cent. In the meantime a marked clinical response occurred essentially all the signs of toxicity disappeared and the patient gained 6 pounds in weight. She remained in the hospital for only 9 days and since then has carried on her work as a housecleaner.

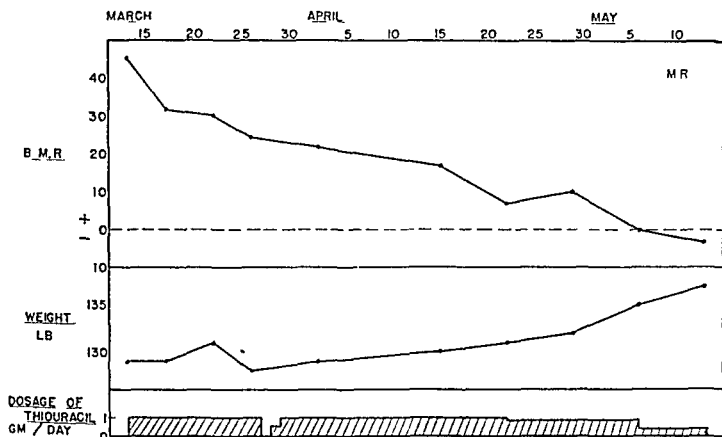


FIGURE 5 Case 5

nal the signs of thyrotoxicity had disappeared and the thyroid gland had assumed an essentially normal size and consistency. There was a gain of 9 pounds in weight, but this occurred chiefly after the metabolic rate had become normal.

During the 2nd week of treatment the patient developed a very slight macular eruption. The phenobarbital that he had been taking was permanently discontinued and thiouracil was omitted for 1 day. The rash lasted only 2 days and did not recur in spite of the resumption of her usual dosage of thiouracil.

Throughout most of the course of treatment the patient has continued carrying on her household duties.

CASE 6 W F (No 1103790), a 50 year-old Negro woman laborer, was admitted on April 19, 1943. Two years previously she had become nervous, with marked restlessness, excitability and emotional instability. In spite of a normal ingestion of food, she lost 44 pounds of body weight in 2 years. She usually had two bowel movements per day, although sometimes she had five or six. She noticed some puffiness of the eyelids but no exophthalmos. For 2 years she had had a fullness in the neck.

On physical examination the patient was restless, apprehensive and excitable. She cried several times during the examination. The skin was loose but otherwise not remarkable. There was palpebral edema and slight impairment to convergence, but no exophthalmos. The thyroid gland was enlarged to three times normal size, and was nodular and firm. The pulse rate was 96 and the blood pressure 170/80.

The thyroid gland has not shown much change in size but is a little softer. She is now taking 0.2 gm of thiouracil three times daily.

CASE 7 R F (O P D No 434179), a 48 year-old housewife, was first seen on March 29, 1943. She had been somewhat nervous ever since her husband's death 6 years previously. However, she dated the onset of most of her thyrotoxic symptoms to a fire in her home 1 year previously, following which she became distinctly more restless, excitable and hyperkinetic and noticed a tremor, palpitation, exertional dyspnea, a goiter and a stare. She had been losing weight for 4 years but during the past year had done so more rapidly, the total being 50 pounds in the 4 years.

On physical examination the patient was moderately restless and excitable. The skin was hot and slightly moist. There was a stare, lid lag and a slight impairment of convergence, but no exophthalmos or other eye signs. The thyroid gland was about three times normal size, firm and nodular and a bruit was audible. The pulse rate was 100 and the blood pressure 140/75. The basal metabolic rate was +53 per cent.

Hospitalization was advised but the patient had so many duties at home that this could not be arranged. On March 31 she began taking 0.2 gm of thiouracil five times daily. Metabolic rates determined at weekly intervals were +55, +38, +22, +19, +15 and +7 per cent. During this time the clinical response was in accord with the changes in the metabolic rate. All evidence of thyrotoxicity had disappeared. The patient

has gained 9 pounds in weight. The eye signs have disappeared. The thyroid gland has shown a distinct decrease in size and consistence but is not yet entirely normal. On May 12, when the basal metabolic rate was +7 per cent, the dosage of thiouracil was reduced to 0.2 gm. three times daily.

Throughout the course of treatment the patient has carried out her usual housework for a large family.

CASE 8. R.J. (No. 1101981), a 49-year-old Negro woman, was admitted on April 2, 1943. Six years previously she had developed exertional dyspnea. This increased progressively and she found it necessary to sleep on two pillows. Subsequently she developed edema of the legs. Two years previously she became nervous, had three to four bowel movements per day, began to lose weight (a total of 40 pounds), developed swelling in the neck and became sensitive to heat. In July, 1941, she was hospitalized for a myocardial infarction. At that time the blood pressure was 160/90. There was mild congestive heart failure. While in the hospital the patient was found to have thyrotoxicosis with a basal metabolic rate of +31 per cent. She took potassium iodide, with a definite improvement in the clinical state and the metabolic rate. However, after a few weeks she discontinued the iodine and had an exacerbation in her symptoms.

On physical examination the patient was restless, excitable and apprehensive. The skin was moist, warm and fine. There was slight exophthalmos and palpebral edema. The thyroid gland was about three times normal size, firm and nodular. The pulse was rapid. The blood pressure was 190/100. There was slight cardiac enlargement but no congestive failure. The urine contained a small amount of albumin, a few white cells and an occasional red cell.

On April 3, the basal metabolic rate was +55 per cent. Two days later the patient began receiving 0.2 gm. of thiouracil every 4 hours. Examination of the urine showed that she excreted an average of 300 mg. of thiouracil daily during the period of 2 weeks' observation.

The basal metabolic rate at 10-day intervals was +55, +32, +22, +22 and +14 per cent. All symptoms of thyrotoxicity disappeared within 4 weeks. During that time the thyroid gland became definitely smaller and softer. The eye signs were never striking and did not show much change under treatment.

The patient was maintained on a daily dosage of 1 gm. of thiouracil for 5 weeks and the dosage was then reduced to 0.6 gm. daily, given in three doses.

Two weeks after she first began taking thiouracil she developed slight swelling of the legs. Urine examination gave the same findings as on admission and there was no evidence of heart failure. The serum protein was normal, but there were 118 milliequiv. of chloride per liter of serum. The carbon-dioxide combining power was 43 vol. per cent. In spite of continuation of the drug the edema disappeared within a few days and the chloride returned to normal, although the carbon-dioxide combining power remained slightly low (41 vol. per cent). However, the latter had also become normal within 2 weeks.

CASE 9. L.S., a 31-year-old woman, was first seen on March 31, 1943. Three years previously she had developed the manifestations of severe thyrotoxicosis. A thyroidectomy was performed in August, 1941, and another

in October, 1941, followed by a disappearance of the thyrotoxic state. However, 1 year later, during the 2nd month of her seventh pregnancy, the symptoms recurred. She became nervous and intolerant to heat. She noticed an increased prominence of the eyes, swelling of the eyelids, burning and itching in the eyes, tightness in the neck and palpitation. She lost 10 pounds in weight in 6 months, in spite of her pregnancy.

On physical examination the patient appeared only mildly toxic. The skin was slightly moist and hot. The eyes showed slight exophthalmos, with palpebral edema. There was about twice as much thyroid tissue as normal and the gland was of firm consistence. The fingers and tongue had a fine tremor. The pulse rate was 100. The basal metabolic rate was +36 per cent on March 31. On that date treatment was begun, using 0.2 gm. of thiouracil five times daily. She was not admitted to the hospital but came to the Out-Patient Department at weekly intervals. The metabolic rate fell to +27 per cent within a week, remained at that level for 3 weeks and then fell to +12 per cent, which is a normal level for a person 8½ months pregnant.

Clinically, the patient was free of all thyrotoxic symptoms within 3 or 4 weeks. The thyroid gland decreased to almost normal size and became softer. No definite change in the eyes resulted. She is now being maintained on 0.2 gm. of thiouracil three times daily.

DISCUSSION

Absorption, Distribution, Excretion and Dosage

We have found, by the methods of Williams, Kay and Jandorf,⁷ that thiouracil is rapidly absorbed and rapidly excreted. For example, to one normal person we gave 0.2 gm. of thiouracil and collected blood and urine samples at the following times: Fifteen minutes, thirty minutes, hourly through eight hours, two-hourly through twelve hours and twenty-four-hourly through three days. The highest blood level was found at fifteen minutes and was 2.3 mg. per 100 cc. Thereafter it fell rapidly until at eight hours only 0.3 mg. of the drug was present, but it did not entirely disappear from the blood until the third day. The most rapid rate of excretion of the drug in the urine occurred during the second hour, 15 mg. being excreted. Thereafter the rate decreased rapidly, only 12 mg. being excreted during the second twelve-hour period, and a total of 6.3 mg. during the second and third days combined.

When thiouracil is given in doses of 0.2 gm. at four-hour intervals, it requires about twenty-four hours to reach a more or less constant rate of excretion in the urine and a constant blood level. With such dosage the urine excretion is about 300 mg. per day, whereas the blood level is about 3 mg. per cent. When the above dosage has been maintained for several days, thiouracil can be found in the urine for six days or more after discontinuing the drug. When the dosage is 0.2 gm. three or four times daily, about forty-eight

hours is required to attain a more or less constant blood and urine level. Almost all the drug that is in the blood exists in the cells, the concentration in the white cells being many times that in the red cells. However, the latter contain a greater total amount of the drug.

It is obviously difficult to determine the distribution of the drug in the tissues of normal human beings. However, we have studied its distribution in the tissues of 2 patients dying from cerebral hemorrhage and 1 dying from bronchopneumonia. Totals of 1.0 to 3.6 gm. of the drug had been given to these patients. Most of the tissues, including that of the thyroid gland, had from 1 to 3 mg. per 100 gm. (fat-free dry weight). The concentrations in the adrenal glands, bone marrow and pituitary gland were greater than this. We have not been successful in finding thiouracil in any stool specimens.

Although the above studies represent a step forward in the estimation of the most desirable dosage and the intervals at which thiouracil should be administered, many more studies of this type are necessary. It would be particularly worth while to determine the optimum level of saturation of the thyroid gland and the dosage necessary to maintain this level. We are conducting such studies at present.

It is now our policy in the treatment of thyrotoxic patients, in the beginning, to give 0.2 gm. of thiouracil at four-hour intervals five or six times daily. With moderate clinical improvement and a drop in the metabolic rate, we reduce the frequency of medication to three or four times daily, spreading the interval as much as is convenient. After the metabolic rate is normal, we reduce the dosage to 0.2 gm. once or twice daily. Our present impression is that a dosage greater than this is not necessary and that a smaller amount will probably be satisfactory.

It will take some time to ascertain how long thiouracil should be given to a patient. On the basis of experiments with the use of iodine, although in many ways the two substances are incomparable, it seems advisable to give it for many months without discontinuation. Astwood et al.³ found a recurrence of the disease in a patient although the latter had received thiouracil for about two months before it was discontinued.

Mechanism of Action

As indicated above, the data available at present suggest that thiouracil lowers the metabolic rate by inhibiting the formation of thyroxine. In the 4 cases in which we conducted iodine studies, we found that following treatment with thiouracil

for a few weeks the protein-bound iodine* of plasma reached low normal or subnormal levels. Since the amount of thyroxine or thyroxine-like iodine of the blood is presumably an index to the amount of thyroxine produced in the thyroid gland, it seems clear that in some way thiouracil inhibits thyroxine production. However, the exact mechanism by which this is accomplished has not been elucidated.

On the basis of animal experiments,^{1,2} it was concluded that thiourea did not inhibit the stimulating effect of desiccated thyroid or thyroxine on the metabolic rate. We have investigated this phenomenon in human beings, using thiouracil. Two patients with myxedema were studied. In each case it was established, by methods which need not be mentioned here,⁶ that the myxedema was primary in the thyroid gland. One patient, M.D. (Fig. 6), was found repeatedly to have a basal metabolic rate of about -44 per cent. She was given thiouracil, 1 gm. daily, for ten days, at the end of which time the metabolic rate was -47 per cent. With the continuation of the thiouracil and, in addition, the administration of 1.5 gr. of desiccated thyroid U.S.P. daily, the metabolic rate had risen to -17 per cent after twenty days of the combined treatment. Then with discontinuation of the thiouracil, but continuation of the thyroid, the metabolic rate became -25 per cent. The other patient, B.F. (Fig. 6), was found to have metabolic rates, before any treatment, of -26 and -36 per cent. After she had received thiouracil, 1 gm. daily, for nine days the metabolic rate was -25 per cent. With continuation of the thiouracil and the administration of 2 gr. of desiccated thyroid U.S.P. daily, the rate was -8 per cent. Thiouracil was discontinued for nine days while the thyroid treatment was continued, but no definite effect on the metabolic rate was observed. When thiouracil was again given for thirteen days, it had no effect on the rise of the metabolism induced by desiccated thyroid. Therefore, we may state that thiouracil does not lower the basal metabolic rate of untreated myxedematous patients, nor does it inhibit the response of the metabolic rate to desiccated thyroid.

We conducted an experiment with another patient, M.D. (Fig. 7), to ascertain whether thiouracil inhibits the goitrogenous and hypermetabolic effect of antuitrin T (thyrotropic hormone). The patient selected had been admitted to the hospital because of possible hyperthyroidism. On the basis of clinical grounds, we decided that she did not have a toxic goiter, but we have not completed the

*This is composed of the so-called "D" and "T" iodines, which are essentially equivalent, respectively, to the di-iodotyrosine and thyroxine contents of the plasma.

blood-iodine studies in her case. Particular attention was paid to the changes in the thyroid gland and the metabolic rate, in association with the administration of thiouracil, 1 gm. daily, for a period of twenty-two days. During the first ten

In the 9 cases of thyrotoxicosis reported above, there was a distinct clinical improvement beginning only a few days after the treatment with thiouracil was instituted. This was true whether the patient was hospitalized or was carrying on

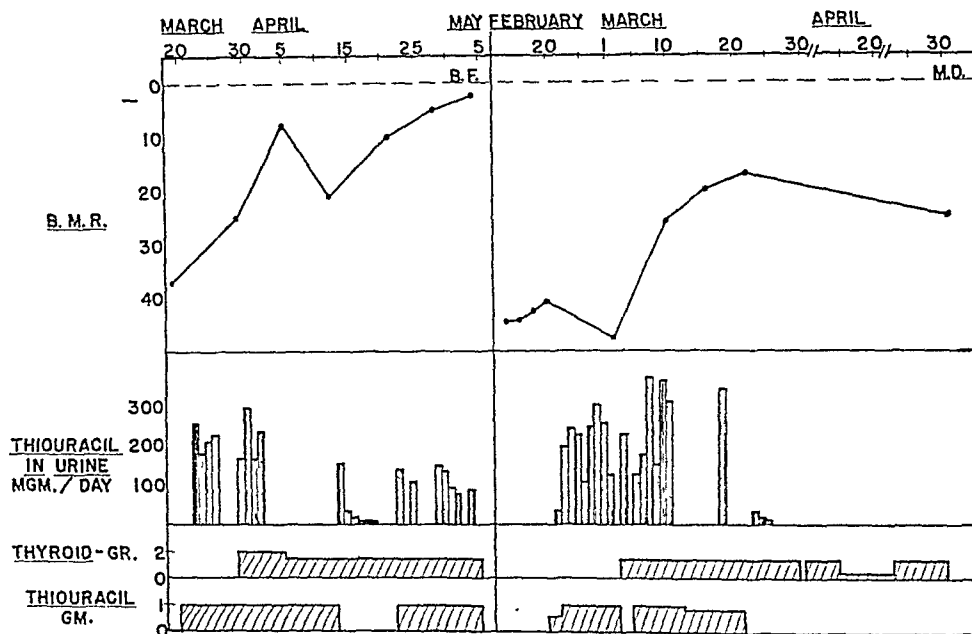


FIGURE 6.

Note that thiouracil had essentially no effect in lowering the metabolic rate of two myxedematous patients and that it did not prevent desiccated thyroid from elevating the rate. Also note the rate of excretion of thiouracil in the urine and the duration of its excretion following cessation of treatment.

days the patient was given daily 2 cc. (50 units) of antuitrin T in sesame oil. Within three days after this treatment was begun the thyroid gland had become definitely larger and firmer. Since the enlargement occurred so rapidly, we believe that it was due chiefly to the thyrotropic hormone injected. The metabolic rate not only failed to rise, but actually showed some decline (Fig. 7). Thus it appears that the thyroid gland had been stimulated to become hyperplastic but that its hypermetabolic effects were inhibited. Finally, the effect of thiouracil was tested in a patient, F.C. (Fig. 7), with a large colloid goiter. The drug was given for seventeen days, 1 gm. daily, but it was found to have no effect on the metabolic rate, or the goiter during this period of observation.

Results of Treatment

Although one is interested in observing any and all effects, good or bad, of thiouracil in the treatment of thyrotoxic subjects, most of the attention is centered on the clinical response of the thyrotoxic manifestations, including particularly the amount of gain in weight; the fall in the basal metabolic rate; the changes in the thyroid gland and the changes in the eyes.

essentially his normal amount of work. Of course, the thiamine,⁹ sedatives, reassurance and other such factors played a distinct role in this accomplishment. This improvement increased progressively until the symptoms of thyrotoxicity had essentially disappeared, within four to seven weeks. Gain in weight, a good index to improvement, took place, most rapidly during the fourth and fifth weeks of treatment.

The fall in the metabolic rate was in close accord with the clinical improvement. In almost all cases the metabolic rate did not fluctuate, but fell progressively downward, in some cases going as low as -15 per cent. A normal level was reached as quickly in severe cases as in the milder ones. Once it returned to normal it tended to stay there so long as the thiouracil was continued.

The changes in the thyroid gland were variable. In 3 patients there was definite, but slight, enlargement in the gland during the first two weeks of treatment. Subsequently the glands returned to their original size. In 2 cases the gland became progressively smaller and softer, finally returning to an essentially normal size. In the other 4 cases it became somewhat smaller and softer than it was originally. In this connection it is significant

that in Case 2 the gland became definitely smaller and softer in association with treatment with desiccated thyroid.¹⁰ This method of treatment has a good rationale because it tends to inhibit the excessive production of thyrotropic hormone, thus

A second possible complication consists of renal involvement. Thiouracil is quite insoluble in distilled or tap water, although it is readily soluble at pH 8.5. We have found no crystals in the urine, no albuminuria and no sedimentary changes.

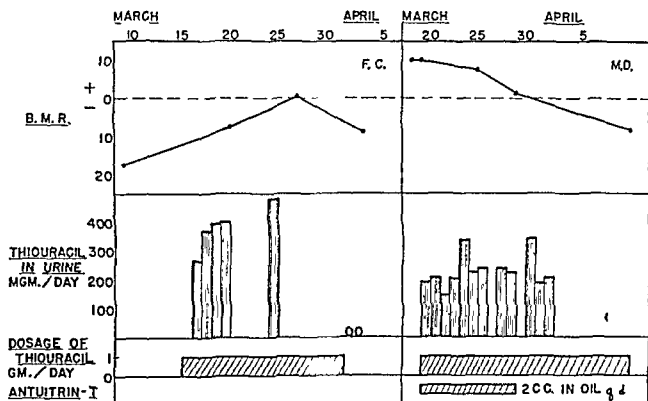


FIGURE 7.

Note that antuitrin-T (thyrotropic hormone) administered with thiouracil caused no elevation in the metabolic rate of a "normal" subject (M.D.). Note also that the treatment of a patient with a large colloid goiter (F.C.) caused no essential change in the metabolic rate. The rate of excretion of thiouracil in the urine should also be observed.

preventing thyroid hyperplasia. We believe that it is partially through this mechanism that desiccated thyroid is of advantage in controlling malignant exophthalmos.⁴ For these reasons, we plan to use thyroid, along with thiouracil, after the metabolic rate has remained within a normal range for a few weeks.

The enlargement of the thyroid gland, associated with thiouracil treatment, that occurred in the 3 cases mentioned above, and the increase in the oculopathy in 1, suggest that in human beings, as in animals, thiouracil leads to excess thyrotropic hormone activity.

Complications of Treatment

The most serious complication thus far observed was the agranulocytosis in a case reported by Astwood. However, his patient was receiving 2 gm. of thiouracil daily, a dosage that is now believed to be unnecessarily high. Yet this is a complication that one must bear in mind, even if a smaller dosage is used, because we have found that the bone marrow takes out a relatively high concentration of thiouracil. We made frequent white-cell counts in our cases, but observed no significant drop.

We have found no essential alteration in the daily urine volume nor in the phenolsulfonephthalein excretion. However, 2 patients developed slight pitting edema with elevation in the serum chloride and a slight fall in the carbon-dioxide combining power. These changes disappeared without discontinuation of the drug and apparently led to no ill effects. Nevertheless, the mechanism of the development of these changes is being investigated.

One patient developed swelling and slight tenderness of the submaxillary salivary glands, which subsided after two days in spite of continuation of the drug therapy. There were no complaints of unpleasantness from the taste of the medicine or general effects from it.

In the patient who was pregnant no ill effects were observed. Furthermore, we have found in rats that saturation of these animals with thiouracil did not interfere with the follicularization or the luteinization induced by pregnancy urine.

SUMMARY

Nine unselected cases of thyrotoxicosis have been treated with thiouracil. In each case the

toxic manifestations disappeared and the basal metabolic rate returned to a normal range. Blood-iodine studies, conducted on 4 patients, showed in each case a fall of the protein-bound iodine to a low normal or subnormal level.

Studies have been performed of the blood levels of thiouracil and its excretion in the urine.

No serious complications from the drug have been encountered, but all patients receiving this drug should be carefully followed.

This report deals only with the early changes resulting from treatment with thiouracil. The results of prolonged treatment will be reported at a later date.

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SPINA BIFIDA AND CRANIUM BIFIDUM*

V. The Arnold-Chiari Malformation: A study of 20 cases

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THE Arnold-Chiari malformation is a congenital anomaly of the hindbrain characterized by a downward elongation of the cerebellum and brain stem into the cervical portion of the bony spinal canal. The condition has been considered a rarity and is unknown to a large percentage of the medical profession. The purpose of this study is to present evidence that it is a frequent accompaniment of myelomeningocele and to discuss the clinical and pathological significance of this relation and other associated findings.

REVIEW OF LITERATURE

The literature on the malformation is limited. The anomaly was originally described by Arnold¹ in 1894 and by Chiari² in 1895. Schwalbe and Gredig³ published an anatomic and embryologic description of it in 1907, including reference to an earlier study by Solovtsoff.⁴

In 1935, Russell and Donald⁵ reported 10 cases of Arnold-Chiari malformation occurring in infants with myelomeningocele. They showed that the anomaly of the cerebellum and medulla in these cases was the prime factor in the production of the complicating hydrocephalus, and suggested that this anomaly might be the mechanism of hydrocephalus in all cases of myelomeningocele and in some cases of simple meningocele.

Penfield and Coburn⁶ in 1938 presented an attractive explanation of the development of the malformation in a case of theirs observed at operation and autopsy. They considered the malformation to be brought about by traction on the brain stem in embryonic life resulting from fixation of the spinal cord at the meningocele site. Normally, growth of the vertebral column and spinal cord occurs at an equal rate until the third month of intrauterine life. After this the bony vertebral canal outstrips the cord in growth, and owing to the anchoring of the cerebrospinal axis by the position of the cerebellum above the foramen magnum, the spinal cord is normally pulled upward so that the conus medullaris comes to lie opposite the first lumbar vertebra. When spina bifida and meningocele are present, the cord may become fixed by herniation and adhesion at the site of the defect so that traction is exerted on the brain stem by the continued growth of the vertebral column and a portion of the hindbrain drawn downward through the foramen magnum. In support of this theory is the observation of Penfield and Coburn that the cerebellar "tails" retracted upward a distance of 3 cm. on being freed from their attachments to the medulla at operation. In their case, and in those of Russell and Donald, the spinal nerve roots in the cervical region were found to pass upward to the intervertebral foramina, rather than horizontally. This was interpreted as additional evidence of a downward traction on the cerebrospinal axis.

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In 1938, Aring⁷ reported a case of cerebellar and brain stem malformation in an adult with cerebellar symptoms without associated hydrocephalus or meningocele. This resembled the Arnold-Chiari malformation anatomically.

McConnell and Parker⁸ in 1938 published a report of 5 cases of hindbrain malformation similar to that described by Arnold and Chiari, but apparently not associated with spina bifida or meningocele. These cases, and that of Aring, tend

ciated with myelomeningocele. The other case was similar to those of McConnell and Parker, and x ray films of the entire spine failed to show spina bifida.

In 1941, List¹¹ included the Arnold-Chiari malformation in an extensive discussion of the neurologic syndromes accompanying bony developmental defects in the occipital region.

Ogryzlo¹² presented 7 cases in 1942. Of these, 3 were associated with myelomeningoceles, and 1

TABLE 1 Data on 20 Cases of Arnold-Chiari Malformation

CASE NO	AGE	SEX	TYPE OF HYDROCEPHALUS	CRANIO LACUNIA	MICRO GYRIA	MYELOMENINGOCELE	HYDRO MYELIA	DIPLO MYELIA	BASEOCCIPITAL DEFECT
240161	1½ yr	M	Block of 4th ventricle	+	+	+	0	+	+
248459	4 mo	M	Communicating	+	+	+	+	+	0
24953*	5 wk	F	Not determined	+	+	+	0	0	+
246581	7 wk	F	Block of 4th ventricle	+	+	+	0	0	0
23804	11 mo	F	Communicating	+	+	+	+	0	0
234581	4 mo	M	Communicating	+	+	+	+	0	+
22230	8 mo	F	Communicating	+	+	+	+	0	+
189446	5 mo	M	Communicating	?	+	+	+	0	0
161359	3 days	F	Communicating	?	+	+	+	0	?
158560	3 mo	M	Communicating	?	+	+	+	0	?
1765	10 mo	M	Communicating	?	+	+	+	0	?
1621	1 mo	F	Not determined	+	+	+	0	0	0
149346	4 mo	F	Block of 4th ventricle	+	+	+	0	0	0
16125	2 days	F	Not determined	+	+	+	0	0	?
1533*	7 days	F	Not determined	?	+	+	?	0	+
									(Klippel Feil deformity)
239648	4 days	F	Communicating	+	+	+	?	?	0
245878	3 mo	M	Communicating	+	?	+	?	?	0
25151	9½ mo	M	Block of 4th ventricle	+	+	+	0	0	+
255724	8 mo	M	Communicating	+	+	+	?	+	+
267425	6 days	F	Communicating	+	+	+	?	?	0

to cast doubt on the traction theory of the genesis of hindbrain malformation, or else suggest that other mechanisms than traction may be concerned in its production. It is interesting that, in Aring's case and in 4 of the 5 cases of McConnell and Parker, spina bifida occulta was not excluded. X ray photographs of the spine were apparently taken in only 1 case and in that one only the lumbar spine was studied and found normal.

In this same report McConnell and Parker described autopsies on 6 infants with myelomeningoceles, 4 of whom had the Arnold-Chiari malformation. In the other 2 there was a "prolongation of flattened cerebellar tonsils through the foramen magnum associated with a nodule on the dorsal surface of the medulla."

D'Errico⁹ in 1939 discussed the surgical treatment of hydrocephalus associated with spina bifida and emphasized the importance of the Arnold-Chiari malformation in the production of hydrocephalus in such cases. He reported 10 cases of myelomeningocele, all of which had an associated Arnold-Chiari malformation.

Two cases were reported by Adams, Schatzki and Scoville¹⁰ in 1941. One of these was asso-

ciated with simple meningocele, whereas the remaining 3 had no overt spina bifida. Again spina bifida occulta was apparently not excluded.

REPORTED CASES

Twenty consecutive cases of Arnold-Chiari malformation that came under observation at the Children's Hospital from 1929 to 1943 were examined. Nineteen of these were studied at autopsy as well as clinically. Their principal clinical and anatomical features are presented in Table 1. All these patients were infants between two days and eighteen months of age. Meningocele, with or without hydrocephalus, was the reason for hospitalization in each case.

The malformation of the cerebellum and medulla in these 20 cases was anatomically identical with Arnold's original case and with those of Russell and Donald. Two parallel tongue-like processes from the inferior poles of the cerebellar hemispheres extended downward through the foramen magnum and were closely applied to the posterior surface of the medulla (Fig 1). In each case from one half to two thirds of the medulla lay below the level of the foramen magnum. The

medulla was somewhat elongated, slightly narrower than usual and flattened anteroposteriorly.

As pointed out by Russell and Donald, the cerebellum was hypoplastic and in most cases lacked differentiation into vermis and lateral lobes. The tail-like prolongations seemed to originate from



FIGURE 1. *Sagittal Section through the Cerebellum and Brain Stem in a Typical Case of Arnold-Chiari Malformation.*

the whole inferior pole of the cerebellum, and in sagittal section appeared to pass down from the nodulus. Microscopic examination of the cerebellar tails shows simply hypoplastic tissue with preservation of the usual cortical architecture.

The fourth ventricle was elongated and flattened. Its lumen was almost obliterated in many cases by the close approximation of the cerebellar "tongue" to the posterior medulla. The foramina of Magendie and Luschka lay below the level of the foramen magnum and were usually identified with difficulty.

In 2 of the cases there was a nodule on the dorsal surface of the medulla, located in the midline and lying just ventral to the lower extremities of the tail-like cerebellar prolongations, or immediately caudal to these. Sagittal sections through

the medulla at this point showed this nodule to represent an exaggeration of the normal structural relations of the most caudal extremity of the fourth ventricle, with an overlapping of the upper cervical cord segment by the adjacent medulla.

The choroid plexus lay in the midline on the ventral surface of the cerebellar prolongations, as a rule, and extended down to their caudal ends. The pia-arachnoid was thickened and extremely vascular over the cerebellar tails, and tended to obscure them in the undissected specimen.

The upper cervical nerve roots were found to run upward to the intervertebral foramina in these cases, just as in those of Russell and Donald and that of Penfield and Coburn (Fig. 2).

Myelomeningocele

Spina bifida and myelomeningocele were present in each of the 20 cases of Arnold-Chiari malformation examined. Usually these were large herniations with extensive neural involvement. In the few that were dissected out post mortem and in all these excised ante mortem there were dense fibrous adhesions binding the lumbar myelomeningocele sac to the margins of the defect in the vertebral arches. Frequently the lumbar nerve roots were incorporated in these adhesions.

Hydrocephalus

Internal hydrocephalus was present in each of the 20 cases of hind-brain malformation. Twelve cases were of the communicating type. In 4 there was obliteration of the fourth ventricle by squeezing of the medulla and cerebellar tails into the narrow confines of the cervical spinal canal. In the remaining 4 cases the type of obstruction was not determined post mortem and no definite conclusion could be reached by re-examination of the fixed brain.

From the work of Russell and Donald and from the examination of the brains in this series it appears that hydrocephalus may be produced by the Arnold-Chiari malformation in several ways: First, the fourth ventricle or the foramina of Luschka and Magendie may be mechanically obstructed by the squeezing of the medulla and cerebellar tails into the narrow cervical spinal canal. Obstructive hydrocephalus results. Secondly, with less severe traction and constriction the relatively unsupported subarachnoid space may be obliterated at the level of the foramen magnum by pressure of the herniated hindbrain, whereas the fourth ventricle remains patent. The foramina of Magendie and Luschka come to lie below the level of the foramen magnum, allowing free passage of fluid to the spinal subarachnoid space, but no egress from the latter to that of the posterior fossa is possible because of the block at the fora-

men magnum. Communicating hydrocephalus results. Thirdly, owing to the traction on the brain stem there may be mechanical irritation of the arachnoid of the basal cisterns with the production of an aseptic inflammation and plastic exudate that

distinctly smaller than usual, and more numerous. "Wormy" is the most descriptive term for these small convolutions.

The exact nature of microgyria of the diffuse cortical type is not well understood, nor is its



FIGURE 2. *Anterior View of the Spinal Cord at Autopsy in a Case of Arnold-Chiari Malformation.*

Note the upward course of the cervical nerves and the lumbar diplomyelia. The myelomeningocele was located in the lumbar region.

block passage of fluid from the spinal to the cerebral subarachnoid space.

Microgyria and Craniolacunaria

Two findings that have not been described previously in the literature as occurring with the Arnold-Chiari malformation are microgyria and craniolacunaria. In all 20 cases examined there was conspicuous microgyria. The cerebral gyri were

relation, if any, to the Arnold-Chiari malformation clear. The fact that it was present in each case examined, however, seems worthy of comment.

Craniolacunaria, or, as it has been called, caput fenestratum, lacunar skull or *Lückenschädel*, was present in 15 of the cases examined. Its absence in the other 5 cases is subject to question, as it is easily missed at routine post-mortem examina-

tion; this is particularly true if the observer is not familiar with the condition.

Craniofacia is characterized by a diffuse involvement of the whole skull with rounded defects of varying size in one or both tables, separated by bony ridges. The defects may be wholly devoid of bone. A study of craniofacia from the roentgenologic point of view has been recently made by Vogt and Wyatt.¹³ These authors found craniofacia present in 52 (43 per cent) of 120 patients with meningocele and discovered that it was more frequently found with myelomeningocele than with simple meningocele.

The etiology of craniofacia remains obscure. Theories concerning its relation to increased intracranial pressure are unproved. Vogt and Wyatt considered it to be an unfavorable prognostic sign in meningocele cases. Whatever its significance may be, its high incidence in Arnold-Chiari malformation seems deserving of notice.

Other Findings

Hydromyelia was present in 8 cases. In each of these the coexisting hydrocephalus was of the communicating type. This relation seems significant as regards the genesis of the dilated central canal.

Bony defects of mild degree in the basiocciput were present in 4 cases, and one of these had, in addition, spina bifida of the atlas. Three cases showed a definite degree of platybasia. In another case there was fusion of the cervical vertebrae suggestive of the Klippel-Feil deformity. These bony anomalies of the base of the skull and cervical vertebrae are apparently not of uncommon occurrence with the Arnold-Chiari malformation, but no developmental relation between the two types of defect has been established.

Three of the cases had diplomyelia, or reduplication of the spinal cord. In all cases the lower thoracic and lumbar regions were involved. Herren and Edwards¹⁴ have recently made an exhaustive study of this anomaly, which they believe represents a certain degree of twinning (Fig. 2).

DISCUSSION

From the study of these 20 cases of the Arnold-Chiari malformation and those reported in the literature there is a striking relation between the hindbrain malformation and low dorsal and lumbar myelomeningoceles. These findings suggest that a high proportion of infants with myelomeningoceles seen clinically may be expected to have a coexisting Arnold-Chiari malformation. An analysis was made of 297 cases of myelomeningocele studied at the Children's Hospital between 1929 and 1942. Of these, 5 came to surgical ex-

ploration of the posterior fossa, and 3 of these were later autopsied. In addition, 15 other cases that did not have cerebellar exploration were examined post mortem. In all 20 cases the Arnold-Chiari malformation was present.

The association of the hind-brain malformation with myelomeningocele, as opposed to simple meningocele, seems to be particularly significant in the light of the traction theory of genesis of this anomaly. A large myelomeningocele is likelier to produce fixation of the cord at the site of the spina bifida than is a simple meningocele, or a meningocele sac containing only a few strands of neural tissue. Hence, if the traction theory is valid, the Arnold-Chiari malformation would be expected to occur far more often with large myelomeningoceles than with simple meningeal herniations.

The cases reported in the literature, as well as those under discussion, offer substantiation of this concept.

Although in all the cases reported the protrusion was low dorsal, lumbar or lumbosacral, it is probable that the same mechanism produces a similar but less marked degree of the same anomalous development in upper dorsal and cervical protrusions. Until this condition is produced experimentally, it is not safe to conclude that the traction theory gives the complete explanation of this phenomenon. The microgyria, craniofacia and other associated anomalies suggest that there is a basic widespread defect. From the information at hand one must conclude that the combination of myelomeningocele, craniofacia, microgyria and Arnold-Chiari malformation constitutes a clinical entity. It is possible that the easily demonstrable radiographic changes of craniofacia will provide a simple clue to the diagnosis.

The preoperative recognition of the syndrome is of great importance in planning a surgical attack on the problem. The long-time results of surgical treatment have not been encouraging, but in properly selected cases surgery is definitely indicated. One should not be misled by a short follow-up in these patients, who may do extremely well for a few months or even years and then suffer from recurrent block in circulation of the cerebrospinal fluid. The history of Penfield's⁶ adult patient provides striking proof that the presence of the Arnold-Chiari malformation does not necessarily interfere with full use of the extremities and mental competence. This patient's circulation of cerebrospinal fluid was presumably in a marginal but satisfactory state of balance for many years and might have remained so except for a slight shift in pressure, which promptly created a vicious circle.

Obviously, surgical treatment should be limited to the patients without extensive paralysis of the lower extremities and sphincters. It should not be offered if hydrocephalus is so advanced that it is inconsistent with normal mental development.

ordinarily follows in ten days to two weeks. If increased intracranial pressure is a problem in this interval, it can easily be controlled by continuous ventricular drainage. In favor of reversing the order of the two procedures is the fact that the

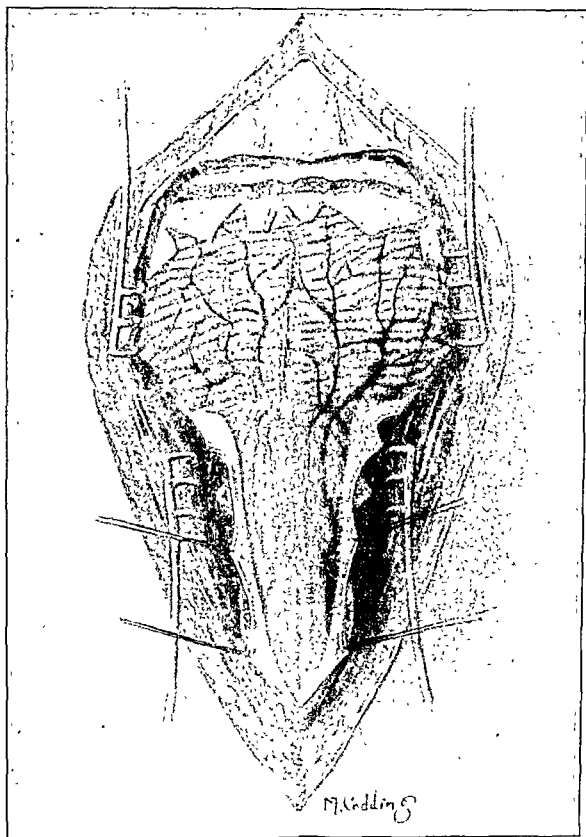


FIGURE 3. *The Arnold-Chiari Malformation as Exposed during Exploration of the Posterior Fossa.*

The exact management of the surgical problem must depend on the particular features of the individual case. In general it has seemed to us more satisfactory to excise the meningocele as the first step, freeing the tissues as thoroughly as can be done without damage to functioning nerve tissue. This usually means only a slight increase in mobility of the spinal cord. The findings at this operation occasionally deter one from carrying out exploration of the posterior fossa, which or-

pressure may remain normal following the cerebellar exploration, thus simplifying the management of the meningocele.

In the exploration of the posterior fossa, which can be carried out by a simple midline incision, the essential feature is a wide decompression, including removal of the occipital bone down through the foramen magnum and laminectomy of the upper cervical vertebrae, continuing down until the cord is exposed and the cerebellar tails are

freed (Fig. 3). This is not a particularly formidable procedure if carried out with due respect for the anomalous venous channels usually present in the dura.

It is hoped that in the future we may be able to select more certainly those patients who should be subjected to this operative procedure. Although it is possible to demonstrate the malformation by air injection, it has not been satisfactory to date to use this method to distinguish the promising from the hopeless cases. Electroencephalography holds definite promise of identifying the associated microgyria, which is probably a contraindication to operation.

SUMMARY

Twenty cases of the Arnold-Chiari malformation associated with myelomeningocele have been studied, and the literature has been briefly reviewed.

The anomalous development has been strikingly similar in all cases.

The majority of the patients had associated microgyria and craniolacuniae.

The outlook is poor in most cases, but prom-

ising cases should be carefully selected and subjected to surgical treatment.

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MEDICAL PROGRESS

THE MODIFICATION OF INTESTINAL MOTILITY BY DRUGS*

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BOSTON

ALTHOUGH the effect of drugs on intestinal motility is an ancient and well-worn subject of investigation, it is only within relatively recent times that observations have been carried out on untraumatized intestinal loops of normal animals and of man. In such experiments, the artefacts and abnormal responses that attend anesthesia, decapitation, shock and local trauma of the bowels are eliminated, and a truer picture of motility, both in the normal state and as influenced by drugs, is obtained. Procedures using intact intestinal loops are not designed to differentiate the function of longitudinal and circular muscles or to answer similar questions of basic physiologic interest. In evaluating the total effect of a drug on human intestinal motility, however, results of investigations using the intact bowel, particularly

the bowel of man, are of paramount significance. For this reason, emphasis will be placed, whenever possible, on the results obtained from human experimentation.

Even if intact bowel loops in one species are used, considerable variation in the intestinal reaction to drugs can be observed, depending on such factors as the dose and route of administration of the drug, the activity and the content of the intestine at the time of the experiment and the technic used in recording motility. In interpreting the results of any pharmacologic study of intestinal motility, it is therefore necessary to take these factors into account. In particular, the advantages, disadvantages and properties of different technics must be understood before apparently contradictory observations can be correlated.

Five general methods are used in recording the motor activity of the bowels in situ. These are direct observation, roentgenologic and fluoroscopic studies, kymographic recording by balloons, re-

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cording by devices attached to smooth-muscle groups, and recording of intraenteric pressures.

“Direct observation (O).”* The intestinal movements may be observed with the naked eye or by photographic means. Usually the intestinal loops are surgically exposed, but occasionally the intestinal activity within a thin-walled hernial sac may be studied. The method eliminates nonphysiologic stimuli within the bowel, but external stimuli resulting from surgical exposure are not excluded. The greatest disadvantage of this technic arises from the fact that the complexity of intestinal movements makes accurate interpretation extremely difficult.

Roentgenologic and fluoroscopic studies (X) With this method, the normal physiology of the intestinal tract is least disturbed, although the question may be raised whether the bowel handles the barium suspension in a manner similar to its handling of foodstuffs. On the other hand, this method merely shows the end result of several interacting forces that may or may not give an indication of the motility of the organ under investigation. For example, the rate of gastric emptying, which is often used as a criterion of the stomach's motor activity, may be delayed by high intraduodenal pressures as well as by gastric atony.

“Kymographic recording by balloons (B).” Balloons can be inserted within a hollow viscus and its contractions recorded kymographically by various means. A balloon method free of objectionable features has yet to be devised, since the presence of the balloon in the intestines serves as a constant and abnormal source of stimulation. Furthermore, balloons occasion more or less intestinal obstruction, are nondispersible boluses in organs that for the most part transport dispersible liquids, and are subject to a variety of influences besides those of local muscular contraction. Nevertheless, the fact that the balloon method lends itself to graphic recording is a tremendous advantage, and if used with due consideration of its limitation, this method yields important results. Balloons can be inserted in intestinal loops that have been opened by surgical means, or they can be used in the intact bowel of man by the Miller-Abbott technic of intestinal intubation.

Recording by devices attached to smooth-muscle groups (M). In surgically exposed loops of bowel, recording devices can be attached to muscle groups of varying size and extent. This technic is precise and allows the action of longitudinal and circular muscles to be differentiated.

*This and the other four symbols denote the method employed in the experiments cited.

On the other hand, it requires surgical procedures and by itself gives no indication of the forces within the bowel.

Recording of intraenteric pressures (P). This method has been attempted by only a few investigators^{1,2} and no complete pharmacologic studies have yet been carried out by this method. Before the full picture of a drug's effect on intestinal motility can be drawn, however, its effect on intraluminal pressures as well as on muscular activity and transport of contents must be studied.

Not only method but phraseology has suffered from lack of standardization. In order to avoid confusion, the following definitions of terms used in this review are given:

Transport. The advance of intestinal contents, whether chyme, barium, balloons or other material, is referred to as transport.

Tone. The tone of the intestine is considered to be the caliber that it maintains in the face of a distending force. This force may vary considerably depending on the method of investigation.

Waves. A tremendous number of terms have been used to describe the wave patterns created by intestinal motility. The most desirable terminology is one that labels waves with letters or numerals and avoids the implication that wave patterns and their effect on transport are identical. Unfortunately, this terminology is limited to methods employing graphic recording. In this review, which includes material obtained by nongraphic methods, wave patterns will be divided into “propulsive” and “mixing” types. Under the heading of propulsive waves fall such terms as “peristaltic waves,” “mass peristalsis,” “Type II waves” of the colon³ and “L waves” of the small intestines,⁴ whereas mixing waves include “rhythmic segmentation,” “Type I waves” of the colon and “S waves” of the small intestine. The adjectives “propulsive” and “mixing,” as used here, describe wave patterns and do not necessarily indicate propulsion or mixing of intestinal contents. Thus, under certain conditions, no transport may occur even when propulsive waves are in evidence, and vice versa, chyme may flow downstream when only mixing waves are present.

Motility. This term, often used incorrectly as synonymous with “transport,” refers to the total spontaneous muscular activity of the intestine. The three component parts of motility—tone, propulsive waves and mixing waves—interact to exert a certain force on the intestinal

contents. Actual transport, however, depends not only on the forces created in any one intestinal area but also on the motility and intraluminal pressures of adjoining areas. As a general rule, a low tone and frequent propulsive waves of large amplitude are conducive to transport, whereas a high tone, which eliminates effective "diastole" between waves,⁵ or a low tone with absent propulsive waves, or inco-ordination of adjoining intestinal segments,³ retards transport. In many reports, motility is called propulsive or nonpropulsive depending on its effect on transport.

GENERAL EFFECTS OF DRUGS

When the intestine is subjected to a pharmacologic action, tone, propulsive waves and mixing waves may be uniformly affected, or the drug may act predominantly on any one of these factors. If this important concept is kept in mind, many apparent contradictory pharmacologic effects will be explained. Thus, a drug may stimulate motility by inducing a marked spasm—that is, high tone—but for reasons given above, it will decrease transport. Vice versa, a drug may decrease motility by reducing both tone and wave activity, but if the major effect of the drug is on tone, transport of intestinal contents may be increased. Quite apart from their specific effect on intestinal motility, drugs may influence transport in other ways. If transport is inhibited because an unco-ordinated motility obtains in two adjoining intestinal areas, exhibition of a drug may co-ordinate motility and facilitate transport regardless of the specific action of the drug. Another possible factor, about which little is known, is the effect of drugs on the quality and quantity of intestinal secretions and on the speed of absorption. If these are changed, intrainstestinal pressures vary accordingly, even if motility is constant, and the rate of transport may be altered. Considerations such as these show why it is most difficult to determine the actions of a drug merely by observing its effect on intestinal transport.

Drugs may influence intestinal motility through a variety of routes. Some affect the irritability of the musculature directly. Others mimic, enhance or inhibit the action of the humeral agents that are believed to transmit impulses from the nervous end organs to the effector cells. As a rule, drugs that favor the transmission of cholinergic (parasympathetic) impulses stimulate motility, whereas drugs that favor the transmission of adrenergic (sympathetic) impulses depress motility. The supposedly reversed effect of these agents on the intestinal sphincters plays a very minor role in controlling transport of intestinal contents. Quigley

and his associates⁶ have shown, for instance, that gastroduodenal pressure gradients, which reflect gastroduodenal motility, are of more importance in controlling gastric emptying than is an independent action of the pyloric sphincter (P).

DRUGS RETARDING TRANSPORT

Morphine

The confusion and contradiction concerning the action of morphine and its related alkaloids on intestinal motility have gradually been cleared away during the past decade. Much of the credit for this achievement belongs to Quigley, Highstone and Ivy,⁷ who urged that propulsive be distinguished from nonpropulsive motility, and to Abbott and Pendergrass,⁸ who demonstrated the feasibility of using the intact small bowel of normal man for pharmacologic studies.

When clinical doses of morphine are injected subcutaneously, a marked rise in tone involves the whole intestinal tract within a few minutes. In the human duodenum, the increase in tone is of sufficient intensity to obliterate the lumen (B and X).⁵ Concomitant with this tonal spasm, the amplitude of the mixing waves is decreased but their frequency is increased; whereas propulsive waves are completely abolished, partly because of the high tone that prevents diastolic relaxation. Similar but less prompt and striking changes occur in the jejunum and ileum. Except for an initial spurt caused by the rising tone, transport is almost completely abolished. The characteristic duodenal spasm that follows the administration of morphine may, in fact, reverse the direction of transport and may play a part in the nausea that at times attends this drug's exhibition (B and X).⁸

After a period of about thirty minutes, the tone of the small intestine drops to a low level and remains depressed for four hours or even longer.⁹ Propulsive waves continue to be absent. As a result, transport, which is initially delayed by spasm, is subsequently delayed by atony.

The response to morphine of the human ileum at or near an ileostomy is also characterized by an increase in tone, increased frequency of mixing waves (M)⁹ and a decrease in propulsive motility (B).¹⁰ In these cases the effect of morphine is more pronounced, and the increase in tone of longer duration (two to three hours), than is found to be the case in the normal intact ileum.⁵ An ileostomy may, however, considerably alter ilcal function, as may the disease for which the ileostomy is performed. Hence, the observations made on the intact viscus are probably more indicative of the small bowel's response to morphine.

The careful studies (B) of Adler, Atkinson and Ivy^{10, 11} show that the colon of both man and the

dog react to morphine in roughly the same fashion as does the small bowel. Nonpropulsive motility—that is, the tone and the amplitude of mixing waves—is increased, but propulsive motility is strikingly diminished. In the colon, however, the elevated tone persists for two to three hours. Whether a late fall in tone ever occurs has not been reported.

Animal experimentation in recent years has yielded consistent results in that morphine is generally found to have a stimulating effect on intestinal motility, but in other respects the observations are more variable. It is, for instance, recorded that morphine abolishes peristaltic waves (B),¹² increases the amplitude of peristaltic contractions (B),¹³ and produces intermittently recurring tonus waves (O).¹⁴

Human experimentation is not invariably attended by consistent results,¹⁰ and at times some areas in the colon may be relaxed while the greater part of this organ is exhibiting a high degree of nonpropulsive motor activity (B).¹⁷ Nevertheless, the evidence is unequivocal that in man morphine usually increases tone and decreases propulsive motility. In the small intestine, a period of atony succeeds the period of hypertoncity. Whether spasm, atony or lack of segmental co-ordination obtains, however, the result is the same: transport of intestinal gas and chyme is seriously retarded.

The clinical application of these facts is clear. Unless morphine is needed for its unsurpassed analgesic action, it should not be used in treating nausea and vomiting, conditions in which intestinal transport is already seriously deranged. Nor, contrary to some opinion, is morphine to be used for the express purpose of treating or preventing paralytic ileus. In patients with partial mechanical obstruction, morphine may relieve pain by abolishing the marked fluctuations in intraenteric pressures produced by huge propulsive waves, and the initial increase in tone may elevate the basal intraenteric pressure (P),² but expulsion of the trapped contents will not be furthered. In this connection, it may be added that the duodenal spasm that attends the use of morphine often makes therapeutic intubation of the small intestine very difficult. If possible, therefore, intubation should be attempted before heavy doses of morphine are given.

Heroin, Diluidid, Pantopon, apomorphine and codeine have the same qualitative effect on intestinal motility as does morphine (X).¹⁶ (B).¹³ ¹⁷ ¹⁸ The action of codeine and apomorphine is relatively weak, whereas 1 to 2 mg of Diluidid produces the same results as does 8 to 10 mg of morphine (B).¹⁰

Papaverine, unlike the other opium alkaloids, is known to inhibit motility. In man, its intravenous injection usually reduces the tone of the colon (B),¹⁸ but most studies on the intestinal effects of this drug have been confined to excised intestinal strips.*

Adrenalin

Intestinal motility should theoretically be inhibited by adrenalin or other sympathomimetic drugs and by drugs that antagonize the action of cholinergic nerves. The use of adrenalin for this purpose is unfortunately of little avail. In the first place, the results obtained with adrenalin are often variable and unpredictable. Not infrequently it has been reported to exert a stimulating effect on motility, most recently by Wells et al.,¹⁹ who noted that intra-arterial injections of adrenalin increased the circular contractions in the distal colon of animals (B and M). In other loops of the dog's colon (B),²⁰ and in the small intestines of dogs (B)²¹ and man (O),²² the reaction is more what one would expect, in that a constant intravenous injection of adrenalin causes a decrease in tone and an inhibition of wave activity. After a period of two to three minutes, however, intestinal motility breaks through this inhibiting effect, even though the injection rate of the adrenalin is accelerated.

Although subcutaneous injections of adrenalin have at times induced relaxation in the human bowel (B),²³ no clear cut or consistent effects are usually observed. This is true of the intact human small intestine (B)²⁴ as well as other preparations. The usual explanation advanced for the inability of adrenalin to effect intestinal motility is that clinical doses that might be effective elicit marked cardiovascular responses.²⁵ Youmans,²⁶ ²⁷ however, has shown that the dog's intestine (B), particularly if sensitized by denervation,²⁸ responds to intravenous adrenalin in amounts that are less than the minimal pressor dose. Hence, the variable response of intestinal motility to subcutaneous administration of adrenalin may be partly due to the bowel's tendency to escape from the influence of a constant supply of this drug.

Amphetamine

The search for a sympathomimetic amine that specifically inhibits intestinal motility has not yet borne fruit. Some hope was held for amphetamine (Benzedrine) because it appeared to relax spasm and enlarge the lumen of the small and the

*Batterman²⁹ in studying the actions of the synthetic substance 1-methyl-4-ethyl-piperidine-4-carboxylic acid ethyl ester hydrochloride (Demerol) found that human intestinal motility is depressed by this drug. A review of the literature by Batterman and Himmelfach³⁰ reveals, however, that this spasmolytic effect is not always obtainable.

large bowel (X).²⁹ This observation was partially confirmed (X)³⁰ and also contradicted (X).³¹ Balloon records of the human small intestine show that if any response attends the exhibition of amphetamine sulfate (15 to 20 mg.), this response tends to consist of a moderate reduction of tone and wave activity (B).³² In half the cases, however, motility is unaltered. The reactions of the human colon are no less equivocal; only occasionally is tone depressed and the amplitude of propulsive waves lessened (B).^{15, 32, 33} Local application of a 0.5 per cent solution of amphetamine sulfate to the human rectal mucosa, examined by means of a proctoscope, is also without motor effect.³⁵

Atropine

Atropine, when used in clinical doses, depresses all phases of intestinal motility. On this point, almost all recent studies concur, whether carried out in dogs (B)^{11, 36, 37} or in man (M),⁹ (O),²² (B)³³ and (B and X).³⁸ Although the efficacy of atropine in inhibiting intestinal motility varies with the dose, 0.6 mg., given subcutaneously, is usually sufficient to lower tone, abolish propulsive waves and decrease the amplitude of mixing waves in the small bowel of man (B and X).³⁸ In the human colon, similar results are obtained with 0.75 mg. (B).^{15, 33} Interestingly enough, the effects of atropine are more marked in the distal than in the proximal colon of the dog (B).¹¹ From the fact that the uniformly depressed tone is unrelieved by propulsive waves, it can be deduced that transport is markedly retarded by atropine.

Following subcutaneous injection, the effects of atropine take place in fifteen to thirty minutes and persist for one to two hours. Intravenous administration of the drug elicits more marked effects of more rapid onset; oral administration produces less pronounced changes in thirty to forty-five minutes.

The question may legitimately be raised why atropine, which is such an effective antispasmodic in experimental studies, is often a source of disappointment in clinical use. Two observations may offer a partial answer. It has been known for some time that atropine effectively abolishes a response to injected acetylcholine, but that it is much less effective in counteracting vagal stimulation. Recently this phenomenon has been quantitated in animals with regard to the pelvic nerve (B and M).¹⁹ Whereas atropine inhibited 97.5 per cent of the stimulating effect on colonic motility of intra-arterially injected acetylcholine, it inhibited only 88.6 per cent of the effect produced by stimulating the pelvic nerve electrically. The usual explanation advanced to account for

this discrepancy is that atropine can act to inhibit acetylcholine on cell surfaces, but cannot act on acetylcholine released by nerve fibers, which may end within the cell.³⁴ The problem has, however, been examined further by Youmans and his collaborators³⁵ who have presented evidence that atropine inhibits intestinal motility in amounts less than that needed to inhibit the intestinal vagus (B). On the basis of this and related evidence, they suggest that the motor activity of the intestines is maintained at a basal level by acetylcholine produced by the myenteric plexuses, and that this basal function operates in the absence of stimulation by extrinsic nerves. The administration of atropine, according to this concept, makes the intestinal musculature unresponsive to acetylcholine produced at basal levels but has less effect on the humoral agents released by the extrinsic nerves. If this is the case, one can understand why atropine shows to such good advantage in experimental studies attempted at basal levels, whereas in functional or organic abnormalities of the intestine, in which the extrinsic nerves may play an important role, the results of atropinization are less favorable. On the other hand, the hypermotility of the rectosigmoid that at times follows prevertebral ganglionectomy in dogs is inhibited by intravenous atropine (B).³⁹

The efficacy of an antispasmodic can be tested under other than basal conditions by observing its action on the intestine rendered spastic by a previous or simultaneous injection of morphine.¹⁵ That the hypermotility produced by morphine is in any way analogous to the hypermotility seen in intestinal disorders has not been proved, although one school of thought holds that the action of morphine on the bowel is essentially cholinergic.⁴⁰

To a certain extent, the action of morphine and that of atropine on intestinal motility are antagonistic. In the dog, small doses (1 mg.) of atropine decrease the transient propulsive motility that occurs after a sizable dose (16 mg.) of morphine is given, but the increase in tone and in mixing waves is not affected. Both the propulsive and nonpropulsive motility stimulated by smaller doses of morphine are, however, antagonized by 1 mg. of atropine (B).^{11, 12} If these results are applied to man, it is seen that toxic doses of atropine would have to be used to abolish the spasmotic effect of clinical doses of morphine. Actual experiment bears out this assumption: 0.7 mg. of atropine sulfate only partially inhibits the spasm produced by 8 mg. of morphine (B).¹⁵ Since both atropine and morphine inhibit transport, it is understandable that this effect should be pronounced when both drugs are exhibited together.

Atropine Substitutes

A number of compounds have been synthesized that appear to inhibit intestinal motility without provoking the side reactions characteristic of atropine. Three of these compounds are in quite extensive clinical use: novatropine, Syntropan, and Trasentin. Methylatropine nitrate (Eumydrin) has also been used, especially in the treatment of hypertrophic pyloric stenosis; but although its effectiveness equals that of atropine, its toxicity, at least in mice, is three times as great (M).⁴¹

Pharmacologically and in its effect on the dogs' intestinal motility, novatropine closely resembles atropine (B).³⁷ Trasentin produces a moderate reduction of the colonic tone in man and decreases the frequency and irregularity of propulsive waves (B).¹⁵ It appears to be more effective in this respect than is Syntropan (B).^{15, 33} The problem deserves further study, however, especially since in most investigations Trasentin has been used in an injectable form, a preparation that the manufacturers have discontinued because of its instability.

Syntropan and Trasentin, unlike novatropine, are said to exert a direct muscle-depressing action as well as an atropine-like inhibition of cholinergic impulses (B).^{42, 43} In view of this fact, one might suppose that these compounds could inhibit the motor effects of morphine more successfully than does atropine. Although this expectation was realized for Syntropan in the case of the dog (B),⁴⁴ Trasentin was found to be not quite so effective as atropine in reducing morphine-induced hypertonus (B).¹⁵ There is also evidence that morphine and Trasentin should not be used concurrently,¹⁶ although this combination exerts no noxious effects on respiration in the dog.⁴⁵

DRUGS ACCELERATING TRANSPORT

Prostigmine

Intestinal motility is theoretically stimulated by acetylcholine or its esters, by drugs that inhibit the activity of cholinesterase and by those that antagonize the action of the adrenergic nerves. The most satisfactory drug for this purpose is undoubtedly Prostigmine, which, like physostigmine, inhibits cholinesterase. Unlike physostigmine, however, Prostigmine is practically devoid of any unpleasant side reactions.

When 0.5 mg. of Prostigmine is given subcutaneously the intact human small intestine responds with a moderate increase in tone and in the frequency and amplitude of the propulsive waves (B).²⁴ In patients with stomas of the large and the small bowel, a similar stimulation of motility is observed (B).^{46, 47} In dogs, the effect is more

pronounced in the colon than in the jejunum (B).⁴⁶ Since propulsive motility is augmented (B),⁴⁷ transport is promoted. One may conclude that in the small and especially in the large bowel, Prostigmine prevents areas of atony, stimulates propulsive waves and co-ordinates these two components of intestinal motility to facilitate transport and expulsion of intestinal contents. Little wonder, then, that Prostigmine is the drug of choice in combating ileus or other conditions where a functional derangement of intestinal transport exists.

Prostigmine Methylsulfate, like atropine, is rather slow in taking effect. A definite change in intestinal motility may not take place until ten to thirty minutes after its intramuscular injection. When Prostigmine Bromide is given orally, its effect may not be noticeable for two to four hours.⁴⁷

Schwartz and his co-workers⁴⁶ believe that Prostigmine must exert a direct stimulating effect on intestinal smooth muscle as well as inhibit cholinesterase, because this drug is effective in certain diseases of the digestive tract in which inflammation or anoxia of the intestinal tissues conceivably might impair the humoral transmission of nerve impulses. In support of this belief, they have shown in dogs that repeated intravenous injections of Prostigmine bring about a slight increase in motility even when the animal is atropinized. It is not generally held, however, that Prostigmine has any direct action on the enteric musculature.⁴⁸ In well-established cases of sprue, for example, in which the myenteric nervous system is thought to be damaged, Prostigmine in 0.5-mg. doses may produce no change in the motility of the atonic small bowel (B).⁴⁹

Ergotamine

Ergotamine is generally supposed to block adrenergic excitatory effects specifically.⁵⁰ Darrow,⁵¹ on the other hand, holds that ergotamine primarily blocks the adrenergic inhibitory effects by "a protection of parasympathetic activity or a physostigmine-like action." This theory is particularly germane to the important work done by Adler, Atkinson and Ivy⁴⁷ on the supplementary action of drugs that stimulate intestinal motility (B). These authors found that small doses of ergotamine have no effect on motility of the human colon, but that ergotamine and Prostigmine potentiate each other markedly. If 0.25 mg. of ergotamine is injected with 0.25 mg. of Prostigmine, the stimulating effect on propulsive motility exceeds that following the administration of 0.5 mg. of Prostigmine, and colonic transport is very active. Oral administration of 1 mg. of ergota-

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 29281

PRESENTATION OF CASE

A sixty-four-year-old fisherman entered the hospital because of an "aching pain in the small of the back."

Five weeks before entry while pulling a dory onto the beach, he experienced rather sudden pain in the small of the back and under the left shoulder blade. A physician strapped his back, but this afforded little relief. The pain intermittently recurred, and about three weeks later the backache became gradually more severe and at times on exertion a sharp pain radiated from the back around to the left anterior costal margin. During the week prior to admission the pain became constant and seemed to be in the region of the eighth and ninth dorsal vertebrae. During that time he lost his appetite and felt weak but had no specific gastrointestinal complaints, such as nausea, vomiting, gas, abdominal pain and jaundice. The patient had always been constipated but in the two weeks prior to admission he believed that the constipation was severer. At no time did he recognize bloody or tarry stools. During the previous two months he had lost 15 to 20 pounds.

The family history was noncontributory. For many years the patient had had a chronic cough occasionally productive of small amounts of brownish sputum. At no time was the sputum blood streaked, and repeated sputum examinations were said to have been negative for tubercle bacilli, though "roentgenographic studies showed some trouble in the lungs." Thirty years before entry he had had "bronchitis" and occasional night sweats.

Physical examination disclosed a thin, apprehensive man who complained bitterly of acute, constant, low-back pain. The examination of the heart was normal. There was a 3-cm. firm, exquisitely tender mass at the angle of the left tenth rib. There was dullness with increased voice sounds and bronchovesicular breath sounds at the right apex anteriorly and at both lung bases; fine

moist rales were audible at both lung bases posteriorly. The abdomen was difficult to examine because it was held tense, apparently as a result of the patient's fear of further discomfort. No masses were felt and no tenderness could be elicited. The abdomen was tympanitic, and normal peristalsis was present. There was slight limitation to forward bending of the neck, without pain or a positive Kernig's sign. There was exquisite tenderness over the spinous processes of the tenth to twelfth dorsal vertebrae, with some tenderness of the posterior portions of the tenth, eleventh and twelfth ribs; however, no muscle spasm could be detected. The extended legs were easily flexed on the trunk without pain. The arms and legs were normal except for varicose veins of the legs, more marked on the right. Several examiners felt a superficial, movable lymph node in the left supraclavicular region. The prostate was small and rather hard, but was not tender. No rectal masses were felt. A neurologic examination demonstrated reflexes within normal limits. Vibration sense was diminished at the ankles, more so on the left. Sensation was normal except for hyperesthesia, particularly on pressure upon the twelfth dorsal spinous process and the right tenth rib in the midclavicular line. There was marked longitudinal ridging of the nails.

The blood pressure was 124 systolic, 88 diastolic. The temperature was 98°F., the pulse 80, and the respirations 20.

Examination of the blood revealed a red-cell count of 3,830,000, with a hemoglobin of 70 per cent, and a white-cell count of 18,420, with 86 per cent neutrophils, 10 per cent lymphocytes and 4 per cent monocytes. Twenty-four hours later the white-cell count was 20,400. The urine was normal. A blood Hinton test was negative. A tuberculin (1:50,000 dilution) test was negative. Examination of the sputum and gastric contents was negative for acid-fast organisms. The clotting time was 4 minutes; the bleeding time, 19 minutes. The stools were guaiac positive on two occasions and negative on three subsequent examinations. The nonprotein nitrogen was 28 mg. per 100 cc., the chloride 102.1 milliequiv. per liter, the van den Bergh 0.85 mg. direct and 1.2 mg. indirect, the protein 4.9 gm. per 100 cc., the albumin being 2.3 gm. and the globulin 2.6 gm.—an albumin globulin ratio of 0.88. The calcium was 10.0 mg., the phosphorus 4.6 mg. and the phosphatase 17.6 Bodansky units per 100 cc. A lumbar puncture revealed an initial pressure of 75 mm. of water; the dynamics were normal. The spinal-fluid protein was 51 mg. per 100 cc.; the fluid did not contain cells. The gold-sol curve was normal.

*On leave of absence

An x-ray film of the lower dorsal spine demonstrated marked degenerative changes—spurring and lipping—consistent with hypertrophic arthritis; there was no definite evidence of metastases. The rectum and cecum filled without delay during a barium enema. No evidence of disease of the rectum and large bowel could be demonstrated. A chest roentgenogram revealed that the diaphragm was low in position, and fluoroscopy showed impaired respiratory motion. The lung fields were large and bright and were not involved by disease. The precordial space was large. Both upper lung fields contained string-like areas of increased density with some flecky areas, particularly on the left side. The left hilus was elevated. There was a circumscribed area of consolidation in the anterolateral portion of the left lower lobe close to the diaphragm. The pleura showed evidence of thickening in this region. Far posteriorly on the left side, superimposed on the shadows of the fifth and sixth dorsal vertebrae, was a soft-tissue mass with a sharply defined convex anterior border that blended smoothly with the pleura. It was not visible in the anteroposterior view. The seventh and eighth dorsal vertebrae were slightly wedged, but they showed no evidence of bone destruction. Following a barium meal, examination of the upper gastrointestinal tract showed a normal esophagus. The stomach appeared large, atonic and moderately dilated and contained a large amount of fluid. Barium passed readily through the somewhat widened first, second and third portions of the duodenum with a to-and-fro motion in the second and third portions. Fluoroscopically the duodenum was slightly narrowed near the ligament of Treitz and barium passed through the area in splashes; no actual obstruction was present, and no evidence of intrinsic or extrinsic disease could be demonstrated on the films.

On the eighth day after admission the patient seemed more comfortable, although he had only been treated symptomatically. The swelling over the tenth rib had decreased in size. On the following day, however, he was markedly dyspneic. The back pain, however, had disappeared. The temperature was 101°F. The sclerae were slightly icteric, and the skin had a slight lemon tint. Dyspnea was severe, but the lungs were clear except for crackling rales at the left base. The heart could not be satisfactorily outlined because of moderate emphysema. The neck veins were distended and pulsating but the wrist pulse was regular. The blood pressure was 120 systolic, 50 diastolic. The abdomen was tense and tympanitic. Examination of the blood revealed a red-cell count of 1,040,000, with a hemoglobin of 6.3 gm., and a

white-cell count of 35,000, with 54 neutrophils, 5 per cent metamyelocytes, 9 per cent myelocytes, 16 per cent questionable blast forms, 13 per cent lymphocytes, 2 per cent monocytes and 1 per cent basophils. The platelets were markedly depressed, and there was marked anisocytosis, poikilocytosis and polychromatophilia of the red cells. The blood picture remained essentially the same for the next few days. He gradually became extremely disoriented and died twelve days after admission.

DIFFERENTIAL DIAGNOSIS

DR. RULON W. RAWSON: To summarize, we have a sixty-four-year-old fisherman complaining of an increasingly severe backache, anorexia, weakness and loss of weight. The significant physical findings were tenderness over the lower dorsal spinous processes and over the posterior portion of the lower ribs, a palpable supraclavicular lymph node and terminal jaundice. The significant laboratory findings included a moderate hypochromic anemia that changed to a marked hyperchromic anemia associated with an impressive myelogenous leukemoid picture, a low blood protein and an elevated blood phosphatase. X-ray examination revealed unusual shadows in the left lung field, nothing definite in the gastrointestinal tract and no evidence of spinal metastasis, although the seventh and eighth dorsal vertebrae were wedged.

The finding of a supraclavicular node, two masses in the chest cavity, pain in the back, a myelophthisic anemia and an increased blood phosphatase suggest a widespread neoplastic process with metastases to the lymph nodes, spine, ribs and bone marrow and a primary or secondary carcinoma in the chest. The low total protein points to liver disease, as does the late finding of jaundice. The increased blood phosphatase might have been due to liver metastases, as well as to an osteoblastic reaction around a metastatic lesion in the skeleton. The dilated stomach and duodenum, with the described to-and-fro movements in the distal part of the duodenum, indicate some obstruction distal to the lower third of the duodenum. Primary tumors of the small bowel are so rare that I shall not consider such a diagnosis and shall explain the apparent obstruction on the basis of pressure from retroperitoneal lymph nodes containing metastatic cancer.

The slightly increased spinal-fluid protein with the rather low initial pressure might indicate a partial block due to spread of disease from the involved vertebrae to the spinal canal.

The most obvious diagnosis to make is that of bronchiogenic carcinoma with generalized metastases. Carcinoma of the prostate with metastasis

might give a picture similar to the one presented by this patient. However, with carcinoma of the prostate it is commoner to see definite x-ray evidence of disease involving the pelvis and spine and less common to see metastases to the liver, lungs and retroperitoneal nodes. Lymphoma might also produce this picture. At this man's age the Hodgkin's or reticulum-cell sarcoma types would be the ones to consider. However, the spleen was not described as palpable and only one peripheral lymph node was felt. It is my impression that jaundice is a rare finding in lymphomatous disease. The blood picture is suggestive of a myelogenous leukemia, but I prefer to interpret it as indicative of a myelophthisic anemia due to bone-marrow metastases. My diagnosis is bronchiogenic carcinoma with metastases to the pleura, vertebrae, ribs and liver and to the mediastinal, retroperitoneal and left supraclavicular lymph nodes.

DR. GEORGE W. HOLMES: I find it a rather complicated job for me to interpret even what is said in the text here. I shall try to point out as many of the things as I can. First, I think we can rule out the gastrointestinal tract as a source of trouble. There is nothing in the text that points to disease, and certainly I am not able to see anything in the films.

So far as the spine is concerned, it is obvious that there are spur-like formations, which are not uncommon in people past middle life. I should not expect that to cause any trouble except vague back pain. I do not believe that the "wedge-shaped vertebrae" are of great clinical significance in an old person with marked curving of the spine. If each were accompanied by a widening of the body and a destructive process in the bone, one would have to pay attention to them. I do not see anything of that kind, however, and I am inclined to put little weight on that part of the findings. The anterior margin of the tenth or eleventh dorsal vertebra shows a concave defect. It is not very clear on this film, which is the only one we have. I shall have to leave the spine without giving any help.

The chest shows an obvious lesion. The hilus was said to be high on the left side, which is obvious. That usually means either fibrosis in the lung or a partial collapse of a lobe—something contracting the upper part of the chest. The films also show a good deal of change in the substance of the lung in the upper part of the chest, probably the upper lobe, and at the base there is obliteration of the costophrenic sinus. On the right side I think the diaphragm is normal. The low position may not mean anything or may mean the patient had a moderate degree of emphysema. According to the fluoroscopic examination there

was no marked limitation of the movements of the diaphragm, which one would expect with emphysema.

CLINICAL DIAGNOSES

Metastatic malignancy, primary site undetermined.

Myelophthisic anemia.

DR. RAWSON'S DIAGNOSES

Bronchiogenic carcinoma, with metastases to vertebrae, ribs, liver, pleura and mediastinal, left supraclavicular and retroperitoneal lymph nodes.

Myelophthisic anemia.

ANATOMICAL DIAGNOSES

Adenocarcinoma of stomach, with metastases to pleura, lung, vertebrae, ribs and mediastinal, left supraclavicular and retroperitoneal lymph nodes.

Myelophthisic anemia.

Hematopoiesis of spleen and liver.

Neoplastic thrombosis of small pulmonary arteries.

Pulmonary tuberculosis, healed.

Pulmonary infarct.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: As Dr. Rawson predicted, this man had a myelophthisic anemia. The vertebral and femoral marrow was almost completely replaced by metastatic carcinoma. In these cases the spleen and, if the marrow replacement is widespread, the liver take on the function of manufacturing red cells, and such was the case here. Both the liver and spleen had foci of hematopoiesis. The primary site of the cancer was not in the lung, but in the cardia of the stomach, 1 cm. below the cardiac orifice on the lesser curvature. I suppose that if the patient could have been stood on his head during the x-ray examination it could have been seen. The two positive guaiac tests on the stools furnished the only lead.

A PHYSICIAN: How do you account for a decrease of over 2,000,000 in the red-cell count during his short hospital stay?

DR. CASTLEMAN: A tremendous loss of red cells in nine days certainly suggests hemorrhage, but there was no evidence of it in the gastrointestinal tract or anywhere else.

A PHYSICIAN: Why did he have a white-cell count of 35,000?

DR. CASTLEMAN: That is unusual, but it may be moderately elevated in myelophthisic anemia.

I am quite sure he had nucleated red cells in the smear, which were not recorded. But nucleated red cells are rarely noted in any hematologic examination so I always assume they are there when I want to have them. One other finding was quite interesting and may have had something to do with the distended pulsating veins in the neck: the patient had no pulmonary emboli, but every small artery in the lung was filled either with tumor thrombus or with secondary fibrous thrombosis, so that he had, in the terminal stages, an acute cor pulmonale. A similar case was described several years ago by Brill and Robertson.* In their case also, the primary carcinoma was in the stomach.

DR. RICHARD CHUTE: Was the back pain due to pathologic fracture?

DR. CASTLEMAN: We did not find any major destructive lesion in the vertebra, although there was diffuse tumor destruction in the marrow. When I read the story through I thought of cancer of the pancreas because I have seen a number of cases of cancer of the tail of the pancreas in which the patients had attended the Orthopedic Clinic anywhere from six months to two years, getting one back brace after another until finally the tumor mass was apparent. This man had a number of enlarged lymph nodes about the celiac axis in immediate apposition with the pancreas but not involving it. I am inclined to think that there was direct nerve invasion at that point, which was the source of the pain. That is a guess however.

DR. HOLMES: Is there any reason why the lung hili were high?

DR. CASTLEMAN: Yes; the patient had old fibrotic processes at both bases, which I think quite certainly were due to healed tuberculosis. He also had an area of fibrosis at the left base that looked like a healed infarct of many years' standing.

DR. HOLMES: We have recognized for some time that widespread cancer in the bone marrow can exist without changes in the bone by x-ray. I perhaps should have mentioned that in discussing the case.

DR. CASTLEMAN: There were no liver metastases. The soft-tissue shadow seen on the x-ray film close to the dorsal vertebrae was a metastasis to the sixth rib, which formed an elliptical soft-tissue mass near the costovertebral junction. Similar but smaller metastases involved the ninth and tenth ribs on the left side.

*Brill, I. C., and Robertson, T. D. Subacute cor pulmonale. *Arch. Int. Med.* 60 1043 1057, 1937.

CASE 29282

PRESENTATION OF CASE

A sixty-five-year-old man, a woolworker, entered the hospital because of jaundice and itching of the skin.

He was well until four months prior to admission when he noticed the onset of itching of the skin. He considered this a "yarn itch" since many other workers had had the same trouble and "scratched the hide off themselves." Three and a half months before entry he experienced on two occasions, a week apart, a sudden, cramping, diffuse, lower abdominal pain, which lasted only a few minutes and was not severe enough to double him up or force him to stop working. There was no nausea, vomiting, fever or chills. At about that time he developed a dislike for fatty foods and noticed that his urine had become much darker in color and his stools clay colored, but there was no change in bowel habits. Two and a half months before entry he developed anorexia and felt so tired that he had to give up work. His physician told him that the itch was not "yarn itch" and gave him a lotion; he went to work in a shipyard. Two months before admission his fellow workers noticed that he was jaundiced. The jaundice gradually deepened, and six weeks prior to admission his physician treated him with pills, which were said to have reduced the jaundice somewhat. He denied the use of alcohol or drugs.

There was no family history of jaundice. His mother died of carcinoma of the bowel. The past history was noncontributory.

Physical examination disclosed a fairly well-nourished man who was moderately jaundiced. The scleras were deeply jaundiced. The lungs were normal. A soft systolic murmur was audible at the apex of the heart. The abdomen was soft but there was slight resistance to deep palpation in the right upper quadrant. A smooth, hard liver edge was palpable two fingerbreadths below the costal margin.

The blood pressure was 145 systolic, 75 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a red-cell count of 3,500,000, with a hemoglobin of 12.5 gm. per 100 cc. and a white-cell count of 10,900, with 73 per cent neutrophils. The urine gave a + test for albumin and +++ test for bile; the sediment was negative. A blood Hinton test was negative. The stools were clay colored, soft, formed and repeatedly guaiac negative. The protein was 7.2 gm., the albumin 4.8 gm., and the globulin 2.4 gm.

er 100 cc. The van den Bergh was 6.8 mg. direct, and 9.8 mg. indirect. The prothrombin time was 32 seconds (normal, 22 seconds), the carbon dioxide combining power 15.3 millimols per liter, the chloride 97.0 milliequiv. per liter, the phosphorus 3.7 mg. per 100 cc., and the phosphatase 15.8 units per 100 cc. A cephalin flocculation test was 0 at 24 and 48°C.

A gastrointestinal series disclosed a normal esophagus, stomach and duodenum. No evidence of encroachment on the stomach or duodenal loop by an extrinsic tumor was observed, and there was no infiltration of the duodenum. A film of the right upper quadrant showed no evidence of gallstones. Chest x-rays were negative.

On the sixth day the patient began to run a spiking temperature, ranging from 100 to 103°F. This continued for six days and then subsided completely. The white-cell count varied from 8000 to 12,000. An occasional stool was light brown but most of them were clay colored. On the tenth day duodenal drainage yielded amber fluid containing a few white cells and calcium bilirubin crystals. He continued to be deeply jaundiced.

After preoperative preparation, including saline glucose infusions and water-soluble vitamin K, an operation was performed on the nineteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD HAMLIN, JR.: The first question to decide is whether or not we are dealing with true obstruction or intrahepatic jaundice. The evidence, particularly the laboratory findings and the description of the liver on palpation, is strongly suggestive of obstructive jaundice. Is the obstruction on the basis of tumor or of stone? In favor of the former is the age of the patient and the history of gradual painless onset. Incidentally, the severe itching might be interpreted in favor of obstructive as opposed to intrahepatic jaundice.

The two episodes of lower abdominal crampy pain, although they might be attributed to biliary colic, are so atypical that it is unwise to consider them as such. The laboratory findings enable one to say only that the patient was moderately jaundiced, had a mild anemia of the secondary type and had no evidence of liver damage as evidenced by globulin tests, both as regards amount and qualitatively (cephalin flocculation test). One would like to know whether the low carbon dioxide combining power was a reflection of abnormal carbohydrate metabolism.

The x-ray examination does not help at all, although occasionally a careful study of the duodenum is of great assistance in such cases.

One must attribute the six days of spiking temperature to cholangitis or to infection entirely unrelated to the primary disease. As Dr. Arthur W. Allen has often pointed out, an occasional brown stool in a series of completely clay-colored ones is commoner in association with carcinoma in the region of the ampulla than with stone, a fact that is presumably attributable to necrosis and sloughing of the tumor, which allow some bile to escape.

Thus far the evidence has tended to point strongly toward the diagnosis of tumor in the region of the head of the pancreas or of the extrahepatic biliary tract. But someone ordered a duodenal drainage, and the report came back that calcium bilirubin crystals were present. If the observation was made by an experienced man, that single fact outweighs in my mind all the piled-up evidence in favor of tumor. Of course it is conceivable that the patient may have had both stones and tumor; but if one diagnosis is to be made, the presence of calcium bilirubin crystals in the duodenal drainage causes me to make the diagnosis of common-duct stone a heavy favorite.

DR. CLIFFORD C. FRANSEEN: We approached the problem much as Dr. Hamlin did, believing that a tumor in the region of the head of the pancreas could not be excluded. At operation the liver appeared to have undergone moderate cirrhotic changes. The gall bladder was found to be distended and free of stones. The common duct was dilated to between 2.0 and 2.5 cm. in diameter. There was a fairly discrete mass in the head of the pancreas, contiguous to the wall of the duodenum, which felt to be about 3 cm. in diameter. Its consistence was characteristic of carcinoma. Because of the patient's long-standing jaundice, it was thought that a two-stage procedure should be done. Accordingly a cholecystojejunostomy was performed as the first stage.

Fifteen days later the second stage was carried out. The pylorus, the first and second portions of the duodenum, the distal half of the common bile duct and the head of the pancreas were resected en bloc. It had been hoped that the end of the third portion of the duodenum could be sutured over the cut end of the pancreas, but this proved to be mechanically impossible, and attempts to fit a loop of jejunum against the cut end of the pancreas produced such a sharp angulation of the bowel that its function would undoubtedly have been too greatly jeopardized. This was due to the fact that the cut end of the pancreas lay in an extraordinarily deep hole. Exteriorization of the cut end of the pancreas was therefore resorted to by drainage anteriorly. This seemed the most direct route, especially since drainage through the

right flank would have had to pass beneath the cholecystojejunostomy. A posterior Polya gastrojejunostomy was done.

CLINICAL DIAGNOSIS

Common duct stone?
Tumor of head of pancreas?

DR. HAMLIN'S DIAGNOSIS

Common duct stone?
Carcinoma of ampulla?

ANATOMICAL DIAGNOSIS

Adenocarcinoma of common bile duct.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The specimen received in the laboratory consisted of the distal portion of the stomach, about 10 cm. of duodenum and the head of the pancreas with the distal 5 cm. of the common bile duct coursing through it. The proximal half of the bile duct was dilated, measuring 2.5 cm. in circumference, but the distal half was narrowed to a circumference of 0.7 cm. There the mucosa was roughened and covered with grayish-white granular tissue, which histologically proved to be adenocarcinoma. The tumor invaded the wall of the bile duct and also blocked the opening of the pancreatic duct, which opened into the bile duct just above the sphincter of Oddi. The pancreatic duct was slightly dilated.

Dr. Hamlin placed a good deal of weight on the presence of calcium bilirubin crystals in the duodenal drainage specimen. How valuable is this test, Dr. Jones?

DR. CHESTER M. JONES: The diagnostic value of a study of duodenal contents in these cases has been proved by many years' experience. Like every other laboratory test, however, it is subject to exceptions, and therefore must be interpreted in relation to the clinical picture. If a good specimen of duodenal contents is obtained and it is found that the sediment contains moderate or

excessive amounts of calcium bilirubin and cholesterol crystals, then the diagnosis of biliary calculus is reasonably certain. If a fair number or an excessive number of cholesterol crystals are obtained, then the same diagnosis should be reasonably considered. Where, as in this case, the sediment contains only white cells and calcium bilirubin crystals, then a more detailed examination should be made of the duodenal contents for other elements, and it should be correlated with the clinical picture. Prolonged biliary stasis, such as may occur in infectious hepatitis or in a prolonged period of extrahepatic obstruction, may cause a precipitation of calcium bilirubin crystals and the appearance of small masses resembling casts. When a flow of bile is re-established, these elements are found for a few days, the casts consisting of mucus, detritus and bile-stained material. Not infrequently, particularly in infectious hepatitis, groups of bile-stained white cells are also noted. Under circumstances such as this patient experienced, with prolonged jaundice and a subsequent flow of bile, which must have been obtained when a duodenal drainage was performed, the appearance of some calcium bilirubin crystals and some white cells in the stasis bile is not diagnostic, and too much stress must not be laid on it.

DR. FRANSEEN: The patient did well postoperatively until the fourth day, when bilateral ligation of the superficial femoral veins for deep thrombophlebitis had to be done. Drainage of pancreatic juice from the sinus tract was profuse. On the thirteenth day the patient had a small hemorrhage from the tract and on the thirty-first day a second hemorrhage. He died a few hours later.

DR. CASTLEMAN: The postmortem showed that the space previously occupied by the resected head of the pancreas and duodenum was replaced by an abscess cavity filled with purplish necrotic material that had eroded into the sutured end of the common bile duct and also into the main portal vein. The result was the development of a pylephlebitis, with numerous abscesses of the liver.

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STARVING EUROPE

THE January 9, 1943, issue of the *British Medical Journal* brings forcibly to one's attention the herculean task of relief in Europe that will face the Allied Nations after the war. Most urgent, of course, will be the provision of food and shelter for the millions still living but rendered destitute and starving by the paternal ministrations of the "master race." After this will come medical care of the sick, social reorganization and, as soon as possible, re-establishment of agriculture and industry.

Efforts are, even now, constantly being made to render what aid is possible to the starving in-

habitants of the conquered nations, but the amount that can be sent and the uncertainty of its getting by so ruthless an enemy render the total results pitifully inadequate. The British Famine Relief Committee has estimated the quantities of dried milk and vitamins needed to save the children of Greece and Belgium, and Sweden has expressed its willingness to carry on this relief. Under the present arrangement 100 tons of powdered milk, in addition to the monthly supply under navicerts of 15,000 tons of wheat, will be and has been dispatched to Greece in Swedish vessels, to be distributed by the International Red Cross.

The need, however, is appalling. In Athens, 100,000 out of 1,000,000 have died of starvation and disease. As early as December, 1941, according to the Athens Welfare Center, 9 out of 10 babies were dying in their first six months because of starvation of their mothers and the lack of milk, practically all the cattle having been slaughtered. From eye-witness accounts: "The children had not even the strength to beg, and some had died as they crouched over a grating; they seemed to be asleep, and hours might pass before their companions realized they were dead. . . . Orphans and abandoned children are found wandering in the streets . . . starving, dirty, pale and thin. . . . They stop at nothing to find a bit to eat, searching among refuse and fighting the dogs for something edible." In June, 1942, in one temporary hospital in Athens, four children were found to a bed. In Belgium, the infant mortality has quadrupled since 1939, with the tuberculosis morbidity increased from 30 to 80 per cent. Thus has the world benefited from that famed *Kultur* of which our adversaries are so proud!

The combined medical and nursing resources of the Allied Nations must also be mobilized, for the apocalyptic horsemen still ride together, and pestilence follows famine as surely as famine follows war. Not only is tuberculosis on the increase but malaria, typhus and the enteric diseases will have to be combated, and scientific nutritional measures put into effect.

The state of so much of the world renders it increasingly imperative that this war be won by the nations that are opposing the slave system of society. After the war, all alliances must be assiduously preserved, for a new world will have to be constructed on the ruins of the old. Friendships must be cultivated, and resources must be husbanded, for there will be desperate need of them both.

A SEMICENTENNIAL OF OSLER'S PRINCIPLES AND PRACTICE OF MEDICINE

FIFTY years ago last year, in 1892, there was published by the D. Appleton and Company of New York, William Osler's *Principles and Practice of Medicine*, intended for the use of practitioners and students of medicine. The appearance of the fourteenth edition in 1942, rewritten in large part by Henry A. Christian but still based on the sturdy design and structure established by Osler, marks the vigor and soundness of this book, one of the great contributions to medical literature. As Cushing pointed out in his *Life of Osler*, the work began seven or eight years before the actual publishing of the first edition. Osler, during those years, wrote various editorials for the *Medical News*, of Philadelphia, and thus kept himself in touch with the new and important ideas in medicine, and when he composed his medical masterpiece, he did it with a thoroughness and a sureness of touch that were immediately apparent to all his contemporaries. In addition, he wrote in such a readable form that this book immediately superseded all other textbooks of general medicine, and has continued to hold a place in the field for fifty years. It was based on sound pathology plus a wide knowledge of clinical medicine. Its sale was so rapid that the first printing, three thousand copies, was sold out in two months, an unprecedented sale for a book of this type. A few corrections were made in the second printing of the first edition. Subsequently, there have been issued nineteen editions in English (thirteen published in America and six in England), three and

an appendix in Chinese, and one each in French, German and Spanish.

In the Boston Medical Library a section is devoted to the editions of this book, where there are examples of all the editions with many variants, numbering over ninety. The history of this book should some day be written for in it, if successive editions are examined, will be found the history of the advancements in clinical medicine in the last fifty years. The last edition, rewritten by Dr. Christian, is a worthy successor to a long line of previously published volumes. In honor of this semicentennial volume, the *Journal* extends congratulations to both Dr. Christian and the D. Appleton-Century Company.

MEDICAL EPONYM

WILSON'S DISEASE

The essay "Progressive Lenticular Degeneration: A familial nervous disease associated with cirrhosis of the liver" formed part of a thesis by S. A. K. Wilson (1878-1936). The monograph appeared in *Brain* (34: 295-509, 1912), and the following is a quotation from pages 486 and 487:

Progressive lenticular degeneration is a disease of the motor nervous system, occurring in young people and very often familial. It is not congenital or hereditary.

It is progressive and fatal within a varying period: acute cases may last only a few months . . . the average duration of chronic cases is four years.

It is characterized by a definite symptom-complex, whose chief features are: generalized tremor, dysarthria and dysphagia, muscular rigidity and hyper-tonicity, emaciation, spasmodic contractions, contractures, emotionalism. . . .

Although cirrhosis of the liver is constantly found . . . there are no signs of liver disease during life. . . .

The chief pathological feature of the disease is bilateral symmetrical degeneration of the putamen and globus pallidus, in particular the former. . . .

A constant, essential and, in all probability, primary feature of the pathology of the disease is cirrhosis of the liver, not syphilitic or alcoholic.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY DEATHS

ABBE—ELIZABETH M. ABBE, M.D., of Roxbury, died January 18. She was in her sixty-ninth year.

Dr. Abbe received her degree from Tufts College Medical School in 1909. She was a member of the Massachusetts Medical Society and the American Medical Association.

FRANK—**MORRIS FRANK, MD**, of Roxbury, died June 17. He was in his fifty seventh year.

He received his degree from Harvard Medical School in 1911. He was a counselor of the Massachusetts Medical Society, a member of the American Medical Association and the American Association of School Physicians. He was a staff member of the Beth Israel Hospital, the Jewish Memorial Hospital and the Washingtonian Hospital. His widow and a son survive.

MERCHANT—**RAYMOND F. MERCHANT, MD**, of Vineyard Haven, died June 7. He was in his forty second year.

Dr. Merchant received his degree from Middlesex University College of Medicine. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives.

PHILLIPS—**MAJOR ROBERT T. PHILLIPS**, former Boston physician, died in a Japanese prison camp in the Philippines. He was in his forty second year.

Dr. Phillips graduated from Bowdoin College in 1924 and Tufts College Medical School in 1932, and afterward served on the staff of the Boston City Hospital. He was called into active service from the Medical Reserve Corps several months before the attack on Pearl Harbor and was at Manila when war was declared, following the evacuation of Manila he presumably went to Batavia. Dr. Phillips was a member of the Massachusetts Medical Society and the American Medical Association.

His widow and four children survive, as well as his twin brother, Dr. Richard B. Phillips.

WRIGHT—**ALLEN H. WRIGHT, MD** of East North field died June 17. He was in his sixty sixth year.

Dr. Wright received his degree from the University of Maryland School of Medicine and College of Physicians and Surgeons in 1906. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow and two daughters survive.

MISCELLANY

BREAKDOWN IN EARLY TUBERCULOSIS

Too often we substitute words for action. We repeat the same soul satisfying phrases until we endow them with a magic and totally undeserved quality of being able to accomplish miracles. Miracles do not just happen. What look like miracles generally turn out to be the result of careful planning, devotion to sound principles and an unlimited amount of tenacity and hard work. The early discovery of pulmonary tuberculosis, by which is meant discovery of the disease in a minimal stage, is an empty accomplishment unless it can be followed by thorough treatment without delay. The following abstract of a recent paper (Stein, S. C. Breakdown in early tuberculosis. *Pub Health Nursing* 35:140-142, 1943) is pertinent.

The prevalent opinion that the finding of active tuberculosis in a minimal stage warrants an excellent prognosis is true only when adequate treatment follows at once. Many of the favorable reports have come from sanatoriums where the outlook on minimal pulmonary tuber-

culosis is not the same as that in the clinics at the time of the early diagnosis.

In sanatoriums the number of minimal cases has not increased in direct proportion to the number of cases found on the outside. Failure to see and follow many diagnosed cases may explain this impression. Some patients who reach the sanatorium with minimal disease may show no unfavorable progression even though weeks or months elapsed between the time of discovery and the beginning of institutional care. These are the more resistant cases. Conversely, a significant number of patients found in surveys, and particularly among those in contact with sputum positive tuberculosis, demonstrate low resistance and a rapid progression of their disease before sanatorium care is finally sought and obtained.

In the Henry Phipps Clinic, Philadelphia, Pennsylvania, even though the serious potentialities of minimal pulmonary tuberculosis are recognized and the physicians and nurses endeavor earnestly and persistently to overcome obstacles that prevent adequate care of these patients, results are astonishingly poor. A study of patients with minimal lesions has revealed that almost half developed progressive disease—true of both white and colored patients. Mortality figures were 25 per cent for the colored and 6 per cent for the white patients. Only one of the cases that died had obtained sanatorium care, and then only when the disease had progressed to an advanced stage.

What causes the poor results? The dominant factors will, largely, be applicable to most localities.

First, the diagnosis. It is universally accepted that the x-ray is the most efficient method. Visualizing the minimal lesion is not difficult but evaluation of its status is not so simple or foolproof. There are three categories: lesions whose appearance indicates active, unstable disease; lesions considered of doubtful significance; and lesions whose x-ray appearance suggests that complete healing has occurred.

Determination of the character of a lesion is based to a large extent on experience with previous similar lesions observed over long periods. Interpreting the objective film is a distinctly subjective procedure and is of prime importance since it influences recommendations for treatment. Many chest experts advocate the follow up of contact cases for a period of at least two years after known exposure ceases. It is obviously necessary to follow for a similar period those cases in the second and third categories mentioned to ensure their diagnosis of stability.

Of the nearly 50 per cent of the institute's minimal cases that showed progression of the disease, 86 per cent developed extension within the first year, the remainder within three years. Serial x-ray studies enable the clinician to determine at the earliest time those cases in which the original estimate of the lesion's stability was faulty.

Following the diagnosis a strong rapport between physician, nurse and patient is essential. The psychologic reactions of the patient to his disease and its treatment depend on the confidence he has in his medical advisers. It is difficult to convince a symptomless patient, often one who was found by survey means and not by his own seeking, to accept such 'drastic' treatment as absolute bed rest. He often scoffs at the diagnosis, claims to feel well and refuses to co-operate.

People in contact with sputum positive tuberculosis may submit to examination merely for the comfort of being told they are free of the disease. When their hopes are

dashed and they are confronted with their own unsuspected trouble, they may turn antagonistic and refuse to accept advice.

Again, society has done little to solve the problem of the family head who must leave behind a situation of destitution for the ones he loves by accepting treatment that must necessarily be a prolonged hospitalization.

Assuming that all these deterrents to treatment have been removed, the actual obtaining of hospital care is in many communities still a great problem, growing greater owing to wartime shortages of materials and personnel. Institutions that require positive sputum before admitting a patient are inviting dangerous progression before making available the badly needed bed. The tendency to regard minimal cases lightly and to treat them insufficiently is far too prevalent and often leads to inexcusable relapses. Reliance on the standards of twenty years ago, which call for dependence on physical signs, to determine the stability of lesions defeats the whole purpose of early-diagnosis surveys, since the case without clinical manifestations will receive neglect instead of the treatment and close supervision it deserves.

Early diagnosis is meaningless unless it leads at once to intelligent handling, prompt care and adequate follow-up, with eventual recovery and maximum rehabilitation the goal. — Reprinted from *Tuberculosis Abstracts* (July, 1943).

CORRESPONDENCE

DEPRIVATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held June 28, the Board voted to revoke the license of Dr. Philip L. Manfredi, 903 Beacon Street, Boston, because of gross misconduct in the practice of his profession.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

BOOK REVIEWS

Textbook of Gynecology. By Arthur H. Curtis, M.D. Fourth edition. 8°, cloth, 723 pp., with 401 illustrations. Philadelphia and London: W. B. Saunders Company, 1942. \$8.00.

The fourth edition of Curtis's textbook is a thorough revision of an already excellent book. Not only has the subject matter been brought up to date, but many improvements and additions have been made.

The first 78 pages are devoted to the anatomy of the female pelvis and perineum. This section is a masterpiece and covers the subject thoroughly. The descriptions are clear, and there are many superb illustrations by Tom Jones.

On this foundation the author proceeds to cover the entire field of gynecology in a competent, complete and yet concise manner. Dr. Curtis is a genius at the difficult art of clear and succinct writing. There is no unnecessary verbiage to confuse and weary the reader. Not only medical students but practitioners will find this book an excellent review of the field, and even specialists will enjoy its lucid expositions.

The section on endocrine is rational and intelligent. Proper emphasis is placed on the sulfa drugs in the treatment of gonorrhea and other infections. Conservative treatment is stressed.

The discussion of tumors is extremely well done. Of special note is the statement that "radium treatment is more radical in its effects than surgical removal." Dr. Curtis quotes Robert Meyer as saying that it is impossible to classify ovarian tumors, and then classifies them. Like all such classifications, it leaves something to be desired. Furthermore, the relative frequency of the various types of tumors might well have been emphasized. Dr. Curtis seems a little too conservative in frowning on resection of the ovary. The reviewer believes that the operation is of value in certain cases. Moreover, a waiting policy, when confronted with a sizable ovarian tumor, may diminish the chance of recovery in malignancy, since operation before spread of the malignancy is as important with ovarian neoplasms as it is elsewhere. Pre-operative differentiation is difficult, and if doubt exists, the reviewer is of the opinion that the patient should be given the benefit of that doubt.

The author's discussion of displacements and relaxation is excellent. It is based on his own work and shows the touch of the master. From the detailed instructions concerning the proper method of inserting a pessary to the descriptions of operative technics, this section is a model of medical writing.

There is no mention of vein ligation in the discussion of femoral thrombosis and pulmonary embolism. The treatment of "milk leg" by injection of the lumbar sympathetic nerves is also ignored. Since these constitute important advances in the treatment of not too rare complications of gynecologic surgery, they should certainly be mentioned.

Throughout the book Dr. Curtis's approach is sane, sound and conservative. As Lincoln might have said, "Anyone who wants a textbook on gynecology will find this a good book."

The Anatomy of the Nervous System from the Standpoint of Development and Function. By Stephen W. Ranson, M.D., Ph.D. Seventh edition. 4°, cloth, 520 pp., with 408 illustrations. Philadelphia and London: W. B. Saunders Company, 1943. \$6.50.

The death of the author of this book was a great loss to neurology and America. He had established himself as a leader in the field of anatomy of the nervous system, as well as in neurologic research. Fortunately, the seventh edition was completed before Dr. Ranson's death, and the book is in the form that he would have desired to see it.

This text has become a standard work on the subject, gradually expanding through its numerous editions since 1920. The subject is presented in a dynamic manner, with emphasis laid on the developmental and functional significance of structure. In this edition certain chapters have been rewritten, particularly those on the sympathetic nervous system. The book has been slightly lengthened, and each page was carefully gone over by the author and his colleagues. Many suggestions from neuroanatomists have been incorporated into this edition, and the section on physiology has been considerably expanded. The volume, therefore, replaces previous editions as a text of outstanding value.

(Notices on page xii)

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OLIVER WENDELL HOLMES AND PUERPERAL FEVER

FREDERICK C. IRVING, M.D.

BOSTON

ON THE evening of February 13, one hundred years ago, the speaker before the Boston Society for Medical Improvement had reached the conclusion of his essay "The Contagiousness of Puerperal Fever." He was a small, frail man just about to enter middle age—for he was thirty-four years old—and his name was Oliver Wendell Holmes. His face had lost much of its customary expression of humorous benignity, his sensitive mouth was firm, and the usual twinkle was gone from his eyes; for never had he been so much in earnest. He said:

There is no tone deep enough for regret, and no voice loud enough for warning. The woman about to become a mother, or with a newborn infant upon her bosom, should be the object of trembling care and sympathy wherever she bears her tender burden or stretches her aching limbs. The very outcast of the streets has pity upon her sister in degradation when the seal of promised maternity is impressed upon her. The remorseless vengeance of the law, brought down upon its victim by machinery as sure as destiny, is arrested in its fall at a word which reveals a transient claim for mercy. The solemn prayer of the liturgy singles out her sorrows from the multiplied trials of life, to plead for her in the hour of peril. God forbid that any member of the profession to which she trusts her life, double precious at that eventful period, should hazard it negligently, unadvisably or selfishly!

You need no aid from me to place America's most charming writer in the world of letters, but perhaps you will permit me to recall his position in the Boston medicine of his day and to remind you of his contribution to the arrest of the fearful pestilence that had needlessly destroyed the

lives of so many women in childbed. And perhaps, also, you will allow me to express, however imperfectly, the peculiar affection that his memory inspires in all Boston doctors, and in every student in Harvard Medical School. As professor of anatomy, he evoked a legend that is as fresh today as if he had just bade his final class farewell, and, clutching silently its gift—a silver loving cup—had descended for the last time those thirty-two well worn steps that he had climbed for five and thirty years to instruct, amuse, and delight two generations of his pupils.

When Holmes read his paper on puerperal fever his medical contemporaries knew him as a witty dinner companion, the author of a volume of facile and melodious verse, a well trained and intelligent physician, and a none too successful practitioner. On graduation from Harvard College, after a brief and boring experience with the law, he entered Harvard Medical School, or the Massachusetts Medical College, as it was then called. In 1833 he left medical school temporarily and went to Europe where he spent a little over two years at the University of Paris, then in a position of unchallenged pre-eminence. The great Louis, who originated the statistical study of disease, taught there in those days, as did such other famous men as Dupuytren, Lisfranc, and Velpeau. Of Baron Larrey, the chief surgeon of the Grande Armée, he¹ said, "To go around the Hôtel des Invalides with Larrey was to live over the campaigns of Napoleon, to look on the sun of Austerlitz, to hear the cannons of Marengo, to struggle with the icy waters of the Beresina, to shiver in the snows of the Russian retreat, and to gaze through the battle smoke upon the first charge of the red lancers on the redder field of Waterloo." There, also, he encountered Ricord, who first dis-

¹For citation before the Brooklyn Gynecological Society, May, 1943.

²William Lambert Richardson, Professor of Obstetrics, Harvard Medical School, visiting obstetrician, Boston Lying-in Hospital.

tinguished between gonorrhea and syphilis and who had so little faith in morality that Holmes called him "the Voltaire of pelvic literature . . . who would have submitted Diana to treatment with his mineral specifics and would have ordered a course of blue pills for the Vestal Virgins."

Holmes returned to Boston in 1835, received his M.D. from Harvard in 1836, and immediately began practice. He won the Boylston Prize in 1836 and 1837, on the first occasion with an essay "The Indigenous Intermittent Fever of New England,"³ — malaria — which is a medical classic. In 1838 he was appointed professor of anatomy at Dartmouth Medical School and held that chair for two years. With Jacob Bigelow he edited in 1839 the American edition of Marshall Hall's *Theory and Practice of Medicine*, and three years later he published his essay "Homeopathy and its Kindred Delusions,"³ wherein he demolished by *reductio ad absurdum* the doctrines of infinitesimal dosage and *similia similibus curantur*. He was well established in Boston also as a teacher of medicine, for in 1838 with Jacob Bigelow, Edward Reynolds, and D. Humphreys Storer he founded the Tremont Street Medical School and taught auscultation and percussion, newly imported from Europe, and microscopic anatomy, another novelty in America. So successful was this school, which later gave summer courses to Harvard medical students, and so practical was its clinical teaching, that the university absorbed it in 1847. It is evident, therefore, that by 1843 Holmes not only had behind him an excellent professional education, but also had attained considerable importance as a medical writer and teacher.

When Holmes read his essay on puerperal fever, it is most unlikely that he had ever encountered in his own practice a case of that disease. Moreover, there was no large obstetric clinic in Boston where he could have studied it. At the Boston Lying-in Hospital, then housed in a small building on Washington Street, there were only about twenty-five women delivered each year—not enough material for even a small epidemic. Aside from the city almshouse, known euphemistically as the House of Industry, that was the only hospital where pregnant women were admitted. His interest in puerperal fever, therefore, must have been aroused in some other way. If we read, as Cutter did, the minutes of the Boston Society for Medical Improvement for the preceding fall, we find reports of two doctors and a medical student who had acquired infected hands at autopsies performed on two women dead of puerperal fever. The student and one of the doctors died; the other recovered after a long illness. At that time, also, there were small scattered epidemics in Bos-

ton and the neighboring towns, and a number of these cases had occurred successively in the practices of individual doctors. Such circumstances had led Dr. J. B. S. Jackson⁴ to ask "the opinion of the Society as to the Contagion of Puerperal Fever, and the probability of Physicians communicating it from one patient to another." This suggestion, and these cases occurring in the practices of his colleagues, led Holmes, who had a broad knowledge of medical literature, to quote the authorities of the past. Charles White,⁵ of Manchester, England, said he believed—like most of his predecessors and many of his contemporaries—that childbed fever resulted from retention of the lochia. In 1773, to encourage its escape, he invented "postural drainage," and he devised a jointed bed operated by a ratchet that was exactly like those we see today in every hospital ward; he also constructed a reclining chair to serve the same purpose when the patient got up. Moreover, White was the first to demand cleanliness in the lying-in chamber and to isolate infected patients from those who were well. In 1783, Pouteau,⁶ Holmes noted, had detected the association of childbed fever with erysipelas, as had Robert Ceely⁷ in 1831 and Thomas Nunnelle⁸ in 1841. Alexander Gordon⁹ had made in 1795 the first epidemiologic study of the disease, using as the basis an outbreak that had occurred in his city of Aberdeen; and he confessed to his great chagrin that in some cases he must have carried the contagion from one patient to another. Thomas Denman was well known to all who practiced midwifery. His tiny book of obstetrical aphorisms,¹⁰ published at the turn of the nineteenth century, reposed in the tail-coat pocket of almost every British and American doctor, to be withdrawn and consulted secretly behind the woodshed when one was in a tight place. Denman¹¹ also said in 1801 that the disease might be carried from patient to patient, and he pointed out that foul bed linen and dressings might be the means by which this was effected. Finally, Holmes quoted Sir Thomas Watson,¹² his contemporary and the most distinguished English physician of his day, who only the year before had written: "Indeed, I believe that these cases of puerperal fever occurring in succession to the same practitioner are something more than ordinary contagion, operating through the medium of a tainted atmosphere. I believe them to be instances of direct inoculation."

Thus armed with the recent experiences of his colleagues and with the evidence drawn from his reading, Holmes announced his conviction that puerperal fever was carried from one patient to another, and that the person who conveyed the contagion was usually the physician or the nurse.

He evolved no theories about the nature of the contagion, nor did he speculate about the mode of its transmission. As he said later, "When facts are numerous, and unquestionable and unequivocal in their significance, theory must follow them as best it may, keeping time only with their step, and not go before them, marching to the sound of its own drum and trumpet." He drew up certain rules of guidance. These were: no doctor practicing midwifery must take an active part in an autopsy on a woman dying of puerperal fever; if, however, he should be present at such an autopsy, even though he did not touch the tissues, he must bathe thoroughly, change all his clothes, and allow twenty-four hours to pass before attending a woman in labor; he must adopt the same precautions after treating a case of erysipelas—he would be even wiser if he avoided the lying-in chamber as long as this contact existed; if a doctor had a case of puerperal fever, he should consider his next obstetric patient in danger of being infected by him; if two cases occurred in his practice, he must give up obstetrics for at least a month; and if he had three cases, he must consider them *prima-facie* evidence that he was responsible for the infection. Moreover, he warned, the doctor must inquire diligently concerning the nurses and attendants who take care of his patients; if they had been in contact with cases of childbed fever, they must not be employed. Finally he said, "A private pestilence in the practice of a physician is not a misfortune but a crime."

All of us who love Holmes could conceive no greater satisfaction than to hail him as the discoverer of the contagious nature of puerperal fever. But here, as so many times, cold facts and the printed word prevent, for he was not its discoverer, nor—as we have seen by the array of authorities he himself quoted to prove his point—did he ever claim to be. But his was the first voice raised in America to drive home this appalling truth; and never, in the whole history of medicine, did any advocate plead his case with greater eloquence or with more conviction.

Holmes's essay appeared in the April, 1843, issue of the *New England Quarterly Journal of Medicine and Surgery*, an obscure periodical that soon ceased publication. At the request of his friends, however, he secured reprints; and some of them eventually fell into the hands of Charles D. Meigs and Hugh L. Hodge, both of Philadelphia; had not this happened, the world might then have profited little by his essay, for it would have remained hidden in the files of a defunct medical journal. Thereupon both Meigs and Hodge expressed their unequivocal disapproval of Holmes, his essay, and the idea that doctors could carry in-

fection from one patient to another. Hodge¹³ was courteous and moderate in his statements, but Meigs¹⁴ attacked the Bostonian in a most insulting fashion. "I prefer," said he sanctimoniously, "to attribute these cases to accident or Providence, of which I can form a conception, than to contagion, of which I cannot form any clear idea." From the eminence of his chair at the Jefferson Medical School he glared down at the little New England upstart, and he characterized the statements of Holmes and of those who held the same beliefs as the "jejune and fizenless dreamings of sophomore writers."

To defend his position, Holmes¹⁵ republished his essay in 1855 under the title "Puerperal Fever as a Private Pestilence," and to it he added certain remarks. He was a kindly man and the soul of courtesy, but it is a pleasure to find that when he tried his hand at polite invective he was good at that, too. In noting that his opponents were professors in two of the country's leading medical schools, and that as such their opinions, although wrong, would have a profound effect on their students, he said that these young men "naturally have faith in their instructors, turning to them for truth and taking what they might choose to give them; babes in knowledge, not yet able to tell the breast from the bottle, pumping away for the milk of truth at all that offers, were it nothing better than a professor's shrivelled forefinger."

Charles Delucena Meigs was one of the most remarkable men in the history of American medicine, not because of anything that he personally accomplished—for a careful search of his works reveals not a single contribution to the healing art—but because he was wrong so often on such important matters and in such a violent manner. He was against everything new and he was against everyone who thought that anything new was good. He¹⁶ quarreled with Channing and Simpson over anesthesia in childbirth, and he¹⁷ berated McDowell when he removed ovarian cysts and thereby saved his patients' lives. Yet the world owes him some gratitude, for had he not assailed Holmes in such a bitter fashion the little doctor might never have returned to the attack.

What, in the history of puerperal fever, is the relation between Holmes and Semmelweis? As regards the transmission of ideas, there is no continuity whatever; for Semmelweis, who began his work three years after Holmes's essay, had never heard of the American. Semmelweis was appointed assistant professor in the *Frauenklinik* of the *Allgemeine Krankenhaus* in Vienna in 1846. Soon after assuming his duties he found that the mortality from puerperal fever among the patients delivered by the students was over

twice that among those under the care of the midwives. He also noted that few women died who had been delivered before they entered the hospital or who had entered in premature labor: the common factor was that none of these patients were examined. At about this time his friend Kolletscha died from a wound received in making an autopsy, and he found the same changes in Kolletscha's body as those that he had seen in women who had died of puerperal fever. He thereupon forbade students to come directly from the autopsy or dissecting rooms to deliver women in the clinic, and he ordered that everyone who examined a patient in labor should wash his hands with liquid chlorine or chlorinated lime. He was the first, therefore, to insist on disinfection of the hands at the time of labor; both Watson and Holmes had gone no farther than to advise it when leaving a case, so that one might avoid carrying contagion to the next patient. Immediately there was an improvement, and during the next year the death rate was cut in half.

In 1847 Semmelweis's results were published by Hebra,⁴ his colleague, who followed with a second article in 1849.⁴ It was not until 1861, however, that Semmelweis's book, *The Cause, Concept and Prophylaxis of Puerperal Fever*, appeared. Whatever advantage there is in priority, therefore, belongs to Holmes; although neither he nor Semmelweis, as is clearly shown by the authorities that the Bostonian quoted, was the first to advance the theory that childbed fever was contagious. As long before as 1694, Phillipe Peu,¹⁷ of Paris, had said, "Putrid effluvia, exhaling from wounded men, brought on a fever which killed a great many childbed women who lay in the same hospital"; and he added, "Are not the putrid effluvia, arising from the lochial discharges in lying-in hospitals, capable of producing the same disease?" To Holmes, also, goes the credit for greater eloquence and vigor of expression; his essay is one of the literary masterpieces of medicine. But his premises were based entirely on the experiences of others; he had no personal knowledge of the disease. On the other hand, Semmelweis's conclusions sprang from his own clinical experiments; there was no need to summon other evidence; indeed, the fact that he knew nothing of the existing literature on puerperal fever adds, if anything, even more to his honors.

After Holmes and Semmelweis about forty years went by before epidemic puerperal fever was finally checked. In America the reactionary influence of Meigs and Hodge, and in Europe that of Semmelweis's opponents—led by Scanzoni,⁴ of Prague—continued to cost the lives of countless women. There was more respect in those days for

academic authority, there were fewer professors, and they were vastly more impressive; their *ex cathedra* statements had all the authenticity of gospel. Moreover, if the contagion was really carried from patient to patient, no one had yet demonstrated its nature or how it was conveyed, for the science of bacteriology did not then exist. In 1865, however, Lister,¹⁸ inspired by Pasteur's discovery that micro-organisms caused fermentation and putrefaction, introduced the principle of antiseptis. To him obstetrics is as much indebted as is general surgery, for nine years later Bischoff,¹⁹ of Basle, impressed by what he had seen in England, applied Lister's methods to women at delivery. Further steps toward the control of puerperal fever followed a logical sequence; in 1878 Koch²⁰ showed that bacteria exist on every unsterilized surface, and the next year Pasteur²¹ discovered that the streptococcus caused the most virulent form of the disease. Using the antiseptic technic that followed such progress, Breisky,²² of Prague, was able in 1882 to report that he had delivered eleven hundred women in succession without a single death—then an unheard of record.

Garrigues,²³ the first to introduce antiseptic obstetrics into America, reduced the death rate at the New York Maternity in 1885 from one in sixteen to one in seventy-two; and using the same methods his friend, Richardson,²⁴ of the Boston Lying-in Hospital, reported that during the following year no woman had died of puerperal fever, although for some time the mortality had been one in twenty. Simultaneously occurred the development of surgical asepsis, which was introduced by von Bergmann²⁵ in 1882. Finally, in 1894, came the publication of Tarnier's book, *De l'asepsie et de l'antisepsie en obstétrique*, which, except for a few minor points, described an aseptic regimen that is as sound today as it was fifty years ago.

As we bid farewell to puerperal fever and to Dr. Oliver Wendell Holmes, we are still puzzled by the question, Why did he abandon the practice of medicine? A man of his intellect and professional training, possessing his knowledge of humanity and his store of ready sympathy, seemed blessed with every essential quality that a good doctor requires. Perhaps he was too tenderhearted, for he was always distressed by suffering in any creature. Possibly, also, the fact that he wrote verses caused his patients to distrust him as a doctor. They forgot that the same god held sway over poetry and medicine; nor were they mindful of the fact that one might woo Euterpe and worship Aesculapius, and still be counted faithful to Apollo. Of course, Mr. Emerson, of Concord, was a poet, although at times he was a

little difficult to understand; so was dear Mr. Longfellow, of Cambridge, who wrote those lovely lines about the blacksmith and the chestnut tree; but, then, neither of them was a doctor. New Englanders in those days liked their medical men to be dignified; if they were portentous, pontifical, and prolix, so much the better. It may have been that Holmes's gay, untrameled spirit seemed out of place in the sickroom; it is also possible that the refined ribaldry that colored some of his utterances disquieted his patients. A man²⁶ who had referred in one of his lectures to the old anatomical plates of Spigellius as those "in which lovely ladies display their viscera with a coquettish grace, implying that it is rather a pleasure than otherwise to show the lace-like omentum and hold up their appendices epiploicae as if they were saving. 'These are our jewels,' might well be too light minded to be intrusted with the care of those who were seriously ill. Also, it was rumored that he had once defecated in a "constipated biped with a pain in the back."

The definite break with practice came in 1857, when the *Atlantic Monthly* was founded and "The Autocrat of the Breakfast Table" began its appearance in serial form. From then on, aside from his lectures at the medical school, which continued until his retirement in 1882, he was primarily a man of letters. Perhaps, after all, the real answer lay in a remark he²⁷ made toward the end of his life about his medical friends: "I hope that they are not ashamed of me and do not reproach me for choosing the flowery path of very light literature rather than to chain myself to the heavy tasks of medical practice." And so it happened that Oliver Wendell Holmes is known to history as a poet, essayist, and philosopher, for there are few besides physicians who remember his part in casting out the evil spirit that in those days haunted the lying-in chamber; and so it happened

also that although he is by no means Boston's most famous doctor, he is, without a doubt, the most famous Bostonian who ever practiced medicine.

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CARE OF THE VICTIMS OF THE COCOANUT GROVE FIRE AT THE MASSACHUSETTS GENERAL HOSPITAL*

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THE Massachusetts General Hospital has recently passed through a most instructive experience. On Saturday evening, November 28, 1942, the Cocoanut Grove, a Boston night club, caught on fire. As a result, 491 men and women lost their lives. During the two hours following the onset of the fire, 114 casualties were brought to the Massachusetts General Hospital. The majority of these were dead on arrival, many survived only a few minutes, but 39 lived and were treated.

The patients arrived in various states. A few came in taxis and walked into the hospital. Most were brought by ambulance on a stretcher. Some were carried in unconscious with no visible burns and died a few minutes after entry. A number were competent and lucid, many were maniacal. The surface burns of the early arrivals were limited to the head and hands; the clothing was but little damaged. Nearly all were coughing; some had labored breathing. Eyes, nostrils and mouth were often burned. Both the mucous membranes and burned surfaces of several patients were cherry red in color, indicating some degree of carbon monoxide poisoning. It was obvious almost at once that we were dealing with something more than the problem of burned skin; a severe impairment of respiration also existed. The possibility that there was pulmonary damage due to an explosion was considered until a few victims arrived who were able to give an account of the fire. It was then clear that no explosion had occurred but that suffocating fumes, in addition to flames and hot air, had been inhaled. An increasing proportion of the late arrivals were extensively burned and unconscious; their clothing was charred and soaking wet.

By this time the general pattern of the injuries sustained was established. The surface burns involved the head and hands, and in the exposed areas inadequately covered by clothing such as the neck, back, arms and legs. The arms were sooty and shaggy from ruptured blebs. In some the cherry-red color of the deeper burn

tissue was vivid. Although burns of the upper respiratory passages were absent in many, signs of pulmonary damage were present in nearly all. There were no fractures in spite of the panic at the fire.

Had this not been a war year, the staff of the hospital would have been overwhelmed by many victims. As it was, the hospital in many ways was prepared to receive them.

The hospital's preparedness was due to two of its war activities. First, since Pearl Harbor, the staff had been organized into teams to meet possible bombing disasters; drills had been held. Second, in two research projects, under the auspices of the Office of Scientific Research and Development, the problems of burns had been under investigation in the laboratory and clinic for nearly a year. Many of the staff had taken part in this research program. Newer modes of therapy had been appraised, and finally when a treatment for burns had been selected for use in a disaster the staff was well aware of its use and purpose.

The importance of anticipating a disaster cannot be overemphasized. The casualties reached the hospital on an average of one every fifty seconds. It was necessary to dispose immediately of the dead in order to have room to care for the living. Four medical interns, working in pairs, were stationed at the admitting door to sort out the dead who were taken along one corridor to a temporary morgue. The living were deposited, still on the stretchers, in the rooms and along the corridors of the Emergency Ward. Nurses and interns, usually in groups of four, were assigned to each casualty.

A room of the Emergency Ward had long before been set aside as a storeroom for emergency supplies. Wooden sawhorses were at hand to support the stretchers on. Sets for intravenous injection, sterile goods and ointment, enough to care for two hundred burned casualties, were immediately available.

The hour of the accident was fortunate in that the victims were arriving at the hospital at the time of the evening shift of nurses. Those nurses who were just coming off duty swarmed down to the Emergency Ward to aid those called from duty elsewhere in the hospital. The resident sta-

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of eighty interns and residents were nearly all immediately available. From outside the hospital, medical students, nurses, nurses' aids and college students volunteered in numbers. Members of the nonresident visiting staff assigned to emergency duty, and technicians, were called by the telephone operators. Having at hand classified lists of the required personnel is imperative in such emergencies.

At first the emergency floor was cleared of all other patients. When it was suspected that the casualties might outnumber the bed capacity of the Emergency Ward, one entire floor of the surgical building accommodating forty patients was evacuated according to previous arrangement and set aside as an isolation ward. The former inhabitants of this floor were fitted into vacant places in other wards throughout the hospital. Subsequently a second floor in the surgical building was cleared, but was not needed.

The concentration of the casualties in one area, rather than their dispersal throughout the hospital, has merit. Not only was strict isolation against organisms of the respiratory tract immediately possible, but better supervision of the care of shock and anoxia was permitted. Emergency quarters hastily fitted up in corridors, garrets or cellars have not the facilities of running water, suction, piped oxygen and electric outlets so necessary for the care of the sick.

The treatment of most of the patients was begun while they were still on the stretchers in the Emergency Ward. After they had received an injection of morphine almost at the entrance, their burned surfaces were covered with sterile towels and intravenous fluids were started. The patients were undressed as they were transferred to beds and were wheeled in the beds from the Emergency Ward directly to the isolation floor. Here the burned surfaces were dressed. Members of the staff, doctors and nurses, were dispatched to this floor to carry on the treatment. The resuscitation squad assembled all the anesthesia machines in the hospital for oxygen therapy. By the time the last of the patients was transferred, the entire staff was working on the isolation floor. The patients were divided into groups of four and attended by members of the visiting staff, residents, interns, nurses and students. The responsible staff members of the burn and resuscitation squads acted as consultants for all the groups.

Within three hours of the time of the fire, all 39 patients were settled on the one floor and were receiving, when needed, oxygen for anoxia and plasma intravenously for shock, their surface burns having been protected by the permanent dressings.

The expeditious handling of these casualties was, of course, made possible by an adequate number of doctors and nurses being immediately available, and by the presence of a blood bank and sufficient supplies in the hospital. But the number of the personnel is of secondary importance to having a prearranged plan of action. Without forethought, both in regard to segregation of the patients and the type of therapy to be employed, confusion will reign.

TREATMENT

Prior to the Cocoanut Grove disaster, the members of the staff responsible for the care of burns had advocated a plan of treatment that emphasized primarily the prevention of the threatening complications of any severe burn, shock and infection. Shock can be treated, but it is wise not to allow it to get beyond the impending stage. Infection too can be conquered, but it is safer and more economic to take the pains to guard against it. In general, it had been planned to prevent shock by plasma administration, to guard against infection by strict isolation, aseptic technic and internal chemotherapy and to cover the surface burns with a bland ointment and pressure dressings and not to cleanse or débride them. This plan was adhered to but had to be altered to give precedence to treatment of the lung injuries. Respiratory complications such as the victims of this disaster exhibited had not been reckoned on, and they demanded immediate treatment.

Pulmonary Complications

As the hours passed after the disaster, the succession of pulmonary signs in the patients recalled those encountered in the soldiers of World War I poisoned by phosgene, and were also similar to those seen in the victims of the Cleveland Clinic disaster of 1929. It had been thought that this latter disaster was unique, for with the resulting change in the chemical composition of x-ray film it had not been expected that nitrous gas poisoning would again be encountered in civilian life.

The picture presented by the Cocoanut Grove patients on arrival was startling. The majority were either maniacal or unconscious. At first the mania was mistaken for hysteria aggravated by pain. Subsequently it was realized that in many it was due to anoxia, and that it was comparable to the restlessness and mania encountered in the anoxia of cardiac insufficiency.

Recognition of the part played by each of the three possible causes of such mania—pain, hysteria and anoxia—is important because the rational therapy for each differs.¹ Morphine is the treatment of choice for pain, but it may aggravate hysteria by its cerebral effect, and anoxia by its de-

pression of respiration. Morphine in large doses is a universal recommendation in the treatment of burns, and we employed it routinely, and without proper consideration, on the victims of this disaster. Each patient received $\frac{1}{4}$ gr. immediately on entry. If this did not have a quieting effect, often a second, and occasionally a third, dose was administered. It is probable that the initial dose did not materially depress respiration but did presumably bring comfort by relieving pain. An overdose, however, was certainly given in two or three cases. Respiration ceased in one patient; she was intubated and given artificial respiration with oxygen for a period of five hours, and survived.

Beecher¹ has pointed out that barbiturates given intravenously are better than morphine for the control of hysteria. None were used in these patients because of the large dose or doses of morphine that had already been given.

Obviously, the treatment for mania due to anoxia is the administration of oxygen. To those to whom it could be given it brought relief and quiet. Two patients, however, were so uncontrollable that it was impossible to restrain them to give the oxygen. To one of these, a strong young man, 4 cc. of paraldehyde was given intravenously and it had an immediate quieting effect. The other patient received paraldehyde intramuscularly with a similar effect. It was not given to any other patient, however, because of the fear, perhaps unwarranted, that it might add to the pulmonary irritation, since it is exhaled through the lungs.

Vomiting also added to the difficulty of oxygen administration. A number of the patients, including those who were unconscious, vomited during the early hours after arrival. Constant care had to be taken to prevent aspiration of vomitus. Oxygen therapy would have been carried out more easily in some patients could an intratracheal tube have been passed, but this would have required cocaineization of the pharynx, which was not done because of the fear that vomitus would be aspirated following the loss of sensation.

The anoxia had two causes. The one which played the smaller role was carbon monoxide poisoning. Oxygen with 5 to 7 per cent carbon dioxide was given to the patients with signs of the poisoning. The major cause was pulmonary damage, which prevented the transfer of oxygen from air to blood. The signs of pulmonary damage multiplied hour by hour. Between the third and fifth hours after the accident, when edema of the skin burns became apparent, signs of pulmonary edema were also evident and anoxia was aggravated. Seven patients received oxygen therapy throughout this period, and suction of the upper respiratory tract was needed.

In spite of the edema of the airway and of the lungs, no patients died within the first twelve hours. The mania and vomiting decreased during this initial period and most of the patients subsided into either a coma or deep sleep.

Beginning twelve hours after the disaster, the clinical picture of the respiratory-tract complication assumed an ominous form. Obstruction of the bronchi and large airways menaced life. Seven patients died, all within a period of thirteen to sixty-two hours after the fire and all as a result of anoxia. No patient died after the third day.*

The lungs of the first patient to die had been gradually flooded with progressive edema. Oxygen under pressure was tried without benefit in such cases. The second patient to die, approximately twenty-four hours after the accident, developed acute respiratory failure, apparently due to edema of the larynx. Tracheotomy was done, but without avail. The third patient to die developed similar edema of the larynx, with sudden closure of the glottis. This man was a strapping young Army officer who had walked into the hospital with severe burns of the face, upper respiratory passages and hands. He had been so restless that he could not lie still but insisted on stamping around and waving his hands; such activity probably did not benefit his injured lungs. Within a few hours signs of pulmonary edema were obvious; tracheotomy was of no help. Following insertion of the tube into the trachea, he coughed up a long shred of mucous membrane, indicating severe damage deep in the bronchiolar tree.

The nature of the lung damage became clear after the post-mortem examination of 3 patients. In those patients severely burned about the face there was denudation of the mucous membrane of the nasal passages, mouth and pharynx. There was also obvious damage below the cords of the larynx, with shreds of mucous membrane and exudate heaped up at the upper end of the trachea. The midportion of the trachea was relatively uninvolved, but increased damage was again present at the carina.

The distal part of the bronchial tree showed shreds of edematous, denuded mucous membrane clinging in spots down into the small bronchioles. It was undoubtedly such shreds that several of the patients had coughed up at intervals. Where these shreds were held in situ, signs of occlusion of the bronchus were apparent. Patchy areas of atelectasis alternated with areas of emphysema. In those areas in which obstruction of the bronchus was complete, atelectasis had resulted; where incomplete, sufficient air had passed on inspiration to be trapped and to cause emphysema.

*One patient committed suicide on the forty-second day, a result directly attributable to the disaster.

The burns of the upper air passages were in part due to heat, but it is probable that toxic fumes accounted for some of the pulmonary irritation. One girl with no external visible burn developed moderately severe signs of irritation in the pulmonary tree. The other patients with minor burns of the face and none of the nasal passages, mouth or pharynx developed similar signs of plugging of the bronchioles.

In the patients who survived, this bronchiolar obstruction manifested itself in various ways. Some patients developed typical asthmatic breathing. At times this was relieved by both adrenalin and aminophyllin, and there was therefore undoubtedly an element of bronchiolar spasm, presumably as a result of the inflammation. From day to day, areas of atelectasis alternated with emphysema. Confirmation of the changing physical signs was obtained by frequent roentgenologic examinations. In one patient with no external burns, atelectasis of both lower lobes developed, accompanied by a vital capacity of only 800 cc. Continuous oxygen therapy was necessary for five days. On the ninth day, following postural drainage, she coughed up a large amount of mucocellular material, and the lungs then became filled with air. Throughout this period of atelectasis she was afebrile. There was undoubtedly a plugging of the larger bronchi. No signs of permanent damage have so far resulted.

Tracheotomy was resorted to but was of limited usefulness because the root of the respiratory evil lay distal to the larynx. It was used in 5 cases, only 2 of the patients survived. In one of these the burn of the pharynx was so severe that swallowing was interfered with. Feeding was carried on from the seventh through the sixteenth day by a tube inserted through the nose into the stomach.

The peak of respiratory difficulty passed on the third to the fourth day following the fire. Signs of moisture decreased and the injured air passages opened. Concern for the lives of these patients, however, was not over. Sepsis in the denuded pulmonary tree was still dreaded. Strict isolation of the patients was continued in the effort to exclude contaminating organisms from the respiratory tract, and no clinical or roentgenologic signs of pneumonia occurred. Virulent staphylococci were obtained on culture from the mucocellular material coughed out of the trachea, but no frank abscesses developed. By the end of two weeks the lungs of most of the patients had healed and our vigilance was relaxed. The unhealed lungs of 4 patients, however, kept them in the hospital two weeks longer.

Careful clinical and roentgenographic follow-up of all patients has shown a complete clearing of the lungs in all except 1 patient, who still had an unexpanded area of atelectasis in one lower lobe at one hundred and nineteen days. This patient had only a moderate degree of pulmonary damage and did not require tracheotomy. She was hospitalized for an extended length of time because of her severe surface burns. It is possible that the enforced inactivity was a contributing cause of the residual atelectasis.

Shock

The primary phase of burn shock is generally considered to be neurogenic. An imbalance of the autonomic nervous system results in a relaxation of the vascular tone and therefore in an increase of the capacity of the vascular bed and a drop in blood pressure. Pain is often a cause of this imbalance. Such primary shock was encountered in a few of the patients from the Coconut Grove. One man with moderate burns, who had been soaked by water and thoroughly chilled, had a systolic blood pressure of 80 on arrival. With rest, warmth and morphine his blood pressure promptly rose to normal. But primary shock was confused by anoxia, which tends to raise the blood pressure.

The secondary phase of burn shock comes on more gradually and is caused by the seepage of blood plasma out through the capillaries into the burned area, for the burn creates an abnormal permeability of the walls. Low blood pressure in this phase results from a decrease in the circulating plasma volume and an increase in the viscosity of the blood, the result of hemoconcentration.

The ideal treatment of secondary shock is the constant replacement of plasma as it is lost from the circulation. If this can be done by injection of plasma intravenously, the course of the patient through this phase, which generally lasts for thirty-six hours, will be smooth. If treatment is delayed until the shock state has already been reached, it is more difficult to return the patient's condition to normal. Nearly ideal conditions existed for the prevention of secondary shock in the patients from the Coconut Grove fire. The fire was but a mile from the hospital and all the patients were admitted within two hours of the onset. Adequate quantities of frozen human blood plasma were available in the hospital's own blood bank. The plasma had to be thawed, but to the late-comers was administered intravenously within five minutes of their arrival. Little or no true secondary shock was therefore encountered in any of the patients.

The damage to the parenchyma of the lung, however, created a dilemma so far as the administration of intravenous fluid was concerned. An integral part of the pathologic physiology of a thermal or chemical burn is an increase in capillary permeability in the area burned and its immediate environs. A protein-rich fluid, slightly more dilute than plasma, exudes into the extracellular spaces and out from the tissues where the surface is denuded. Such weeping occurs in burns of the lungs and bronchioles as well as those of the skin, and is responsible not only for the edema of the alveolar and bronchiolar walls but also for the fluid in the alveoli and lumens. The edema and fluid of course cut down the transfer of gases across the alveolar wall, and, when excessive, result in anoxia.

Edema in the burned area may be increased by the intravenous injection of saline or glucose, solutions of small molecules that are freely diffusible through the capillary wall. Such solutions increase blood volume, even transitorily, raise blood pressure, and thereby increase the outflow of the plasma filtrate from the capillaries. Restoration of normal blood concentration and volume by the administration of plasma itself probably also tends to increase the edema of the burned tissues, even though it maintains a normal circulation for the unburned portions of the body. It is possible that if a certain amount of hemoconcentration is allowed to exist, the plasma will seep out of the damaged capillary membrane less readily and edema will be decreased. The blood of the patients with the severe signs of pulmonary damage was allowed to concentrate to some degree. It is not clear whether this hemoconcentration was effective. It was not sufficient to disturb the metabolism of the patient as a whole, since normal kidney and liver functions were maintained.

Surface Burns

The recognition in the last half-century that burn shock is due to plasma loss rather than to absorption of toxin from the burn has created a debate concerning which should be treated first, the shock or the burn. Without proper treatment of shock, the life of the severely burned patient is in jeopardy. To maintain, however, as some still do, that nothing should be done about the burn wound itself until after the treatment of shock has been accomplished is to court trouble.

Neglect of the surface wound means increased bacterial contamination, and contamination means infection. The chief problem of burns is infection, and the most effective way to eliminate infection is to prevent it by covering the wound at the earliest possible opportunity. The importance of

such preventive treatment cannot be overemphasized.

The treatment of the surface wound cannot be divorced from that of shock, for they are interrelated and must go on simultaneously. Infectious toxemia leads to shock, and shock leads to an increased growth of bacteria. Shock from an inadequate circulating blood volume leads to stagnation of blood, particularly in the peripheral tissues, and results in a decrease in oxygen tension. Some organisms, such as certain streptococci, are preferential anaerobes and multiply more rapidly under conditions of anoxia. From the point of view of prevention of infection, therefore, an adequate treatment of shock is imperative, just as is the prompt covering of a burn wound with a protective coating.

One of the drawbacks of the current methods advocated for the treatment of burn wounds is their complexity. It is common practice, both in civilian hospitals and in the armed forces, to débride and cleanse such wounds. Débridement consists of opening all unruptured blebs and cutting away the dead epidermis overlying these blebs and those that have already ruptured. This leaves the dermis exposed, a surface vulnerable to infective organisms. Therefore, such exposed surfaces are gently scrubbed with soap and water or a detergent, and finally rinsed with saline solution. Since such maneuvers may be exquisitely painful, even when deftly performed, anesthesia is often considered necessary. Such débridement and cleansing are conducive to further shock, particularly when accompanied by general anesthesia, and are postponed until the treatment of shock is advanced. Anything that aggravates shock is obviously contraindicated. Such débridement was a necessary preliminary step for the treatment with tannic acid. It has been carried over into other forms of treatment without critical evaluation.

Another relic of the tannic acid ritual, which adds to the complexity of surface treatment, is the two-stage treatment of the burn surface, first-aid and definitive. Débridement and hourly spraying of tannic acid cannot be carried out under first-aid conditions but have to be reserved until operating-room facilities are available. This increased handling is also conducive to shock and is likewise contraindicated.

For several months prior to the disaster the rationale of reducing the treatment of the burn wound to the simplest terms had been explored in the clinic and laboratory of this hospital. Such a simple surface treatment had been tried out, but received its first mass trial on the victims of this fire.

The extent of the surface burn of these patients varied from patches of the mildest first-degree burns to extensive deep burns. The burns of the typical pattern were not extensive but were frequently deep. One third of the patients had burns that were more widespread than the general pattern, and these were deep. Many of the burned areas were grossly clean, others covered with dirt and soot. A number of the patients had been crawling on the floor at the fire or were piled in with the dead. The burns of several were exposed to feces, and many of the patients, dead and living, were incontinent. The eye burns were limited to the lower half of each cornea.

The treatment was carried out as follows: The attendant personnel was carefully masked to prevent the spread of organisms from the upper respiratory tract.* Immediately all exposed burned surfaces were covered with sterile towels. When the patients were undressed and transferred from stretchers to beds, burns of the body were covered by laying sterile sheets on the bed and enfolding the patient in them. On the isolation floor these sterile drapes were removed and the surfaces covered with boric-ointment gauze. The gauze, impregnated with liberal amounts of the ointment and autoclaved, was put on by medical students and interns who wore, in addition to masks, sterile gloves but unsterile gowns. *No débridement and no cleansing of any surface were done.*† Dry sterile gauze was laid over the ointment gauze and pressure bandages were applied to all wounds of the face, scalp and extremities. Sulfathiazole, 5 per cent, in petrolatum was placed in the burned eyes, the lids closed, and the eyes incorporated in the pressure dressings of the face. Only the nostrils and mouth were left uncovered.

As a final but integral part of the surface treatment, 2 gm. of sodium sulfadiazine was injected intravenously into each patient. This was accomplished readily by a technician who injected it into the rubber tubing of the intravenous set, which was already functioning. Subsequent doses of sodium sulfadiazine were given intravenously, or by mouth if the patient could tolerate it.

Such a treatment of surface burns is unorthodox in modern surgery, when one is accustomed to neat wounds. When it was first suggested a year ago that we should not débride a burn wound, this was objected to by those concerned with infection. They believed that all blebs must be opened because otherwise the bacteria harbored in gland crypts would burrow up from the base of the vesicle to infect a fluid that was a fertile anaerobic cul-

ture medium. This objection seemed unreasonable on two counts. In the first place, skin has been shown to have the ability to destroy pathogenic organisms on its surface,²⁻⁴ and it is probable that the gland crypts have the same ability. The only organisms to survive on skin are its natural inhabitants and they are nonpathogenic. These organisms, principally *Staphylococcus albus*, should not lead to an infectious process. In the second place, in the early hours of the burn at least, bleb fluid is in open communication with the extracellular spaces. In 1932, Field, Drinker and White⁵ showed that there is a greatly increased flow of lymph from the area of an experimental burn, suggesting that there is a turnover of fluid in a burn wound. Since the fluid originates in the capillaries, it has the oxygen tension of the blood, and relatively aerobic conditions may well exist in a burn wound until the intercellular spaces become plugged with fibrin. An observation of comparable significance to the increased lymph flow in the dog has often been made in the human being: a débrided burn wound weeps freely, and the protein-rich fluid from the capillaries brings with it a supply of oxygen to the injured tissue.

It remained to be shown in patients with burns that blebs left undébrided did not become infected. Prior to the Coconut Grove disaster, the unruptured blebs of 26 patients, some with several blebs, had been protected from one to fourteen days, after which time the fluid was withdrawn from these vesicles under sterile conditions and cultured. The fluid from the majority of blebs was sterile; from a few the nonpathogenic saprophytic organisms of the skin were recovered, and in only one was a virulent organism, a streptococcus, cultured. In this case alone was the bleb grossly infected. In all the others, healing occurred promptly beneath the unruptured blebs and there was no evidence that the bleb fluid retarded healing.

Again, we were unorthodox and did not cleanse the wounds because we doubt that any cleansing other than vigorous scrubbing materially reduces the number of organisms on the wound. Such scrubbing of delicate, unprotected tissue would presumably result in more extensive injury and as much harm would be done as benefit derived.

A simple bland ointment was applied to the burn surface because, so far as has been determined, such an ointment does not injure the viable remnants of epithelium. Substances such as tannic acid or the triple dyes commonly recommended for the treatment of burns have recently been shown to retard the regeneration of epithelium.⁶ It is possible that plain petrolatum would be as good as or better than petrolatum with boric

*Marking of the patients was impossible because of the respiratory complication.

†The face and left hand of 1 patient were partially débrided and cleansed with soap and water before the general order was understood.

acid. Boric acid, however, may prevent the multiplication of pyocyanous organisms; pyocyanous was conspicuous by its absence in these patients. On the other hand, too rapid absorption of boric acid might result in poisoning. Boron was recovered in the urine of these patients, but no poisoning attributable to its presence was determined.

No substance has been proved to promote epithelial regeneration. It is believed by many that toxins are formed in burn wounds, but their presence has not been substantiated and surface agents designed to eliminate them are, therefore, of questionable value.

A sulfonamide was not incorporated in the ointment, not because we believe that it has an injurious effect on the epithelium but because absorption through the burn wound occurs and may be rapid and irregular and give rise to sulfonamide poisoning.^{7, 8} The sulfonamide administered internally permeates through the burn wound since it is freely diffusible out of the capillary wall. It is possible to control the level of sulfonamide in the body fluids by internal administration and thus prevent poisoning. At this hospital, sulfonamide levels have been demonstrated in bleb fluid equal to those in the blood plasma. Such observations were also made in the patients of the Coconut Grove fire. We are not certain, however, if sulfonamide therapy is withheld for more than forty-eight hours, that an adequate bacteriostatic level in the burn wound would be reached, since the cell spaces eventually become plugged with fibrin.

The original dressings were not changed on any of the patients until the fifth to tenth day, when a boric ointment dressing was reapplied. Full precautions were maintained in a temporary operating room set up on the isolation floor. Later, in preparation for grafting, saline or boric acid solution dressings were used to help liquefy the dry slough of the deep burns.

The main advantage of this surface treatment lies in its simplicity. In a civilian disaster, as in warfare, there is inevitably a disproportion between the number of casualties and the number of trained personnel. This was true in this disaster. The treatment was applied by relatively untrained workers, the skilled personnel of this hospital being free to care for the pressing problem of anoxia and shock. The activities required to apply the dressings were so unobtrusive that the administration of plasma and oxygen was not interfered with. The dressing relieved pain promptly, and all manipulations that tend to increase shock were cut to a minimum. Since the dressing does not interfere with the life-saving treatments and does not increase shock, it could be applied immediately

and therefore contamination and subsequent infection were reduced. It is so simple that hospital facilities, such as an operating room, are not required. The treatment is both first aid and definitive. Once applied, the dressings should not be touched for a week to ten days.

Because of its simplicity, this method of treatment has administrative advantages. It requires no complicated apparatus and nothing that is not used in other types of wounds. Special solutions, spray guns and heaters, all requiring extra space for storage or transportation, are not needed.

The results of this simplified treatment of the burned surface were gratifying. The second-degree or incomplete-thickness burns of the skin healed promptly without evidence of infection. The 17 patients having such burns had all been discharged by the end of two weeks. The only patients remaining in the hospital for a longer period were the 10 with deep or complete-thickness burns of the skin, the 1 with severe damage to the central nervous system from anoxia and the 4 held on account of residual signs of the pulmonary complications.

Early grafting of the deep burns was possible. The sloughing dead skin contained numerous organisms and there were occasional small abscesses beneath the necrotic tissue, but the wounds were remarkable because of the absence of invasive infection. The margins of the skin next to the granulating areas were not ulcerated or inflamed. There was no evidence of cellulitis, lymphangitis or lymphadenitis.

This absence of active infection is to be attributed to the chemotherapeutic program, not to any cleanliness of the burns on arrival. None of the burns were cultured before they were dressed originally because of the exigencies of the moment, so that the actual degree of contamination is not known. The first cultures were taken at the time of the first dressings. Cultures were also taken at subsequent dressings and the course of the bacterial flora was studied until healing occurred. The bleb fluid of unruptured blebs was cultured in many patients and found, as expected, to be sterile. Pathogenic staphylococci were found in almost all open wounds in the first and subsequent cultures, whereas streptococci were almost completely absent. In any similar group of burn patients the latter organism would have been present in the majority as a result of contamination from the respiratory tract. It is fair to believe that the sulfadiazine was responsible for the incongruity of incidence of these two types of bacteria.*

*Although penicillin was administered to 13 patients, it was given in what is now known to have been too small a dose, and it was not started until the sixth day. No decision can be reached regarding its effect for it is possible that the observed results are attributable to the sulfadiazine alone.

The burns of 9 of the patients were grafted. The extent of the surfaces grafted varied from 1 to 28 per cent of the body. The first graft was done on the twenty-third day, the last on the one hundred and twenty-fourth day. The initial graft on 2 patients did not survive, presumably because of the bacterial flora present in the granulations. The subsequent grafts on these patients took, as did all those on the other patients. The first of the grafted patients was discharged on the fortieth day, the next to the last on the one hundred and third day. All patients were discharged healed except for the last one, who was discharged on the one hundred and forty-third day. She was the most extensively burned patient to survive. On discharge there were still a few small granulating points in the grafted areas.

Many of the patients with deep burns of the hands have required physical therapy to restore function.

Clinical proof of the absence of invasive infection in the majority of the granulating areas of these patients is illustrated by the achievement in 1 patient. The skin on the dorsum of one hand was so severely burned that when the slough was cleared away the extensor tendons of two fingers lay exposed. A split graft to this area, had it been able to obtain an adequate blood supply, would have resulted in adherent tendons. Instead, the hand was implanted into the abdominal wall for two weeks. The graft of skin and subcutaneous fat took without incident and the tendons were saved. While the hand was in the abdominal wall there were minimal signs of inflammation. Had there been an active infection in the hand wound, the graft would not have taken and an abscess would have developed in the abdominal wall.

The absence of invasive infection not only permitted early successful grafting but also prevented any extension of the areas requiring grafting. Several deeply burned areas, at first considered to be complete-thickness burns, eventually epithelialized from numerous small islands of the rete. Had there been deep infection such islands would not have survived, and grafting would have been necessary.

Keloid overgrowth has formed in some of the deeply burned, ungrafted areas. It is too early to tell what will have to be done to them. Excision with grafting may be necessary, in which case it would have been wiser to have grafted the areas in the first place.

Pressure dressings have recently been advocated to reduce edema and promote healing. Although all the burns of the extremities, face and scalp were treated in this way, we do not think that we

can commit ourselves concerning its worth. On the extremities, the pressure undoubtedly did reduce the edema, the fluid being expressed upward above the dressings. On the face the fluid was expressed posteriorly to the scalp and then downward into the deep tissues of the neck and over the chest and shoulders. The dressings formed effective splints and, by decreasing the amount of lymph, may have reduced the spread of infection.

Ligation of veins for thrombophlebitis was required in 5 of the patients. The lesion was first suspected in 2 patients by the appearance in chest roentgenograms of areas suggesting pulmonary infarcts. In the other patients, local inflammation was the presenting sign. The cause of the phlebitis in one case was the use of an ankle vein for a constant intravenous injection; the superficial saphenous vein was ligated on the ninth day after the fire. In the other patients there was probably more than one cause, prolonged bed rest with immobility being the most important factor. In two cases, a pressure bandage applied to wounds of the thighs and not started at the ankle was probably a contributing factor. The thrombophlebitis bore no relation to the chemotherapy or the multiple femoral-vein punctures that a number of the patients required for blood studies, administration of plasma and whole-blood transfusions.

SOCIAL AND PSYCHIATRIC ASPECTS

A civilian disaster may induce social or psychiatric difficulties among either the survivors or the relatives of the dead. States of confusion, bewilderment and grief, requiring a psychiatrist's help, were encountered by the social-service workers among the relatives who came to the hospital seeking missing ones. Several of the injured had lost a husband, wife or close friends. One had lost a son and husband, and another, both her parents. Some of these patients made a good adjustment to their grief, others a poor one. All were aided by consultations with the psychiatrist. One patient who had lost his wife voluntarily returned to the hospital two weeks after his discharge for psychiatric care and eventually committed suicide. Although he had previously been an unstable person, his death is directly attributable to the disaster. The wisdom of the Social Service Department in its trained handling of relatives, and its prompt recognition of psychiatric disturbances, were noteworthy.

METABOLIC STUDIES

The numerous studies on blood, urine and feces that were made in order to guide the course of the therapy have yielded considerable information. No patient developed impairment of kidney

function, and this in spite of the fact that hemoglobinuria was present in 9 patients, being massive in 5. Albuminuria was encountered but left no residual.

Metabolic observations were also undertaken. A study of the nitrogen balance was made in 29 patients. In 23 of these the 17-ketosteroid excretion was followed throughout the hospital stay and, in some, longer. In 8 patients the potassium balance was studied. When an adequate nitrogen and caloric intake was possible, nitrogen balance was maintained. The excretion of nitrogen by the kidney was not influenced by the extent of the burn but was influenced by the sex of the patient. During the initial days when there was an inadequate caloric and nitrogen intake, the nitrogen balance was negative but there was not a comparable negative potassium balance. This indicates that the source of the nitrogen was not cellular protein.

The nitrogen deficit was less than anticipated in view of recent reports.⁹⁻¹¹ It is possible that this relatively low excretion of nitrogen may be attributed to the absence of infection in the burn wounds, since it is well known that infections are associated with a rapid excretion of nitrogen from the body.

The excretion of 17-ketosteroids in the urine rose above normal during the first five to seven days and then abruptly descended to a subnormal level; this level was maintained until convalescence was complete. The steroid excretion did not correlate with the changes observed in nitrogen balance. Such a relation has been reported elsewhere, and it is claimed that the adrenocortical hormone is responsible for the excretion of nitrogen by burned patients.¹¹

COMMENT

Many lessons can be learned from the experience with the victims of the Cocoanut Grove fire. Some were known before but their significance has been re-emphasized. The necessity for a prearranged plan of organization, administration and therapy for a large number of disaster victims is obvious.

Three important things in regard to burn therapy were learned. First, lung damage, presumably from both heat and irritating gases, may be an added complication and should be anticipated in any mode of therapy to be used on patients of a civilian fire. Unless one is aware of such a possibility, the meager initial signs in the lungs may be overlooked, and pulmonary edema and sudden death will result. The second thing learned, a corollary of the first, is that the adminis-

tration of morphine in large doses should not be given to burned patients when pulmonary complications exist. If mania is present, anoxia should be excluded as a cause before giving a respiratory depressant, although in burned patients covered with dirt and soot, anoxia may be hard to recognize. Thirdly, the treatment of the burned surface can be simplified, without compromising the care of the wound, by dispensing with débridement and cleansing, provided that adequate chemotherapy is administered. Also, a complicated surface agent is not necessary to obtain gratifying results.

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DISCUSSION

DR. C. R. MULLINS, Concord: I should like to know a few more details of the chemotherapy. What blood levels did you maintain, how often did you have to give the sulfadiazine, and what were the doses?

DR. W. J. P. DYE, Wolfeboro: I should like to ask Dr. Cope a question concerning his method of administration of intravenous sulfadiazine. I had been under the impression that it should not be given at the time of or in conjunction with intravenous saline. Dr. Cope stated that this was administered through the tube in which saline and plasma were being administered.

DR. R. W. ROBINSON, Laconia: For the last two years, in the group where I am practicing, we have been using a 15 per cent phenol and vaseline ointment, without débridement, when dealing with burns, and I am confident that I have never seen any débridement of a surface burn that affords such complete relief or in which the burns heal so quickly and so readily with as little scarring. This was brought to our attention through a Dr. Miller, who has an extensive practice in a West Virginia hospital in the coal-mining district; he has been using this ointment for years. I was a bit hesitant at first because of the fear of phenol absorption and poison. Of course, as an antiseptic phenol is excellent. Furthermore, epithelialization of these wounds takes place underneath the ointment, seemingly at an accelerated rate.

In the beginning we used it in only a few cases, but we came to employ it more and more extensively. Our pathologist covered the wounds of laboratory animals with it, in an attempt to determine whether there was

any evidence of absorption of phenol. There was no such evidence whatsoever. In addition, patients who had been treated with this ointment and who had extensive burns, such as a whole leg or a leg and an arm or the abdomen, showed no evidence of phenol absorption, according to laboratory tests on the urine.

In other words, we have used no chemotherapy with this ointment, because we have had no infection whatsoever in the burned areas since using it.

DR A. L. MACMILLAN, JR., Concord. I should like to ask Dr. Cope to say a word or two about burns of the cornea.

DR COPE (closing). Perhaps I can answer the first two questions together, since they deal with chemotherapy.

All the patients had intravenous tubes in place, as I said. Each patient received 2 gm. of sodium sulfadiazine, injected intravenously by a technician. This was a simple procedure. Sodium sulfadiazine is a soluble salt, it is not like sulfadiazine alone. We have encountered no trouble from its use. It has been adopted as a routine procedure by the doctor who is in charge of surgical infections in our hospital.

The subsequent administration of sulfadiazine was by the continued intravenous route in those patients who could not swallow, and by mouth in those who could swallow. Each patient received an additional 6 gm. of sulfadiazine in the first twenty-four hours, and 4 gm. on the subsequent days, until it was omitted.

A few cases showed red cells in the urine. The blood levels, however, were carefully watched, and ranged between 4 and 10 mg. from the second day on. One patient reached 12 mg. on a single day. In the first twenty-four hours, the dose was not sufficient in 3 patients. Three patients developed sensitivity. One of them developed a drug fever and rash at the end of the second week, and the sulfadiazine was omitted.

Again, I want to emphasize that we consider this a successful therapeutic program. There are many things that enter into such a procedure against infection. First, the burn wound was covered early and protected immediately, thus reducing contamination. Secondly, the wound was not disturbed, reliance being placed on internal chemotherapy. Sulfadiazine was found each time that fluid from an exposed bleb was removed and analyzed and its concentration was equivalent to that in the blood

during the first ten days. However, if internal chemotherapy had been postponed until after forty-eight hours, I doubt that adequate levels in the bleb fluid would have been reached. By forty-eight hours, the intercellular spaces of the burned wound became blocked with fibrin, and passage of substances from the blood into the burned area and the bleb fluid was slowed.

DR DYE. What were the contraindications?

DR COPE. We did not believe that there were any.

As to Dr. Robinson's 15 per cent phenol in vaseline ointment, my objection to this is mainly that such a concentration of phenol undoubtedly damages otherwise viable epithelium, just as tannic acid does, or the triple dyes. A concentration of such a substance as phenol or the triple dyes that is sufficient to prevent bacterial growth is injurious to tissue. The sulfonamides and penicillin have the distinct advantage of being non-injurious to epithelium. They do not impede or retard epithelial regeneration in concentrations adequate for bacterial stasis. In that way, they are a godsend for the treatment of wounds.

As to the absorption of phenol, one might get a false picture by measuring or looking for it in the urine, because phenol is a protein precipitant and is rapidly fixed in the tissues. If any of it should get into the lymphatics, it would almost certainly be combined with protein; in this form, it might not be excreted by the kidneys promptly, yet could cause damage elsewhere. However, I should exclude phenol principally on the fact that it causes further injury. This is equally true for the triple dyes and tannic acid, if the concentration is high enough to keep down the infection. In deep burns that are incomplete when one puts on something that injures the epithelium, a full thickness burn is created and the injury is increased, even to the point of requiring grafting, which prolongs hospitalization. That is the reason why the use of such substances is in my opinion to be excluded.

About the burns of the cornea, there were 12 patients out of the 39 who had bilateral ulceration of the lower half of the cornea. At the Boston City Hospital, patients with burns of the eyes had the identical lesions. The treatment by our ophthalmologist was 5 per cent sulfadiazine ointment in petrolatum, put under the lid, the eyes were then closed, and a pressure dressing applied. The corneas in all the cases healed without scarring.

THE GASTROINTESTINAL SYMPTOMS OF HEART DISEASE*

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MANY persons with heart disease first consult a gastroenterologist because of symptoms of indigestion. On the other hand, an equal number consult a cardiologist because of symptoms that suggest heart disease but in reality arise from the gastrointestinal tract. Not infrequently the physician himself finds it difficult to decide on the source of the symptoms.

CONDITIONS ENCOUNTERED

Congenital Abnormalities

Gastrointestinal symptoms may arise from congenital abnormalities of the cardiovascular system. A right-sided aorta, a rare anomaly, causes difficulty in swallowing by pressure on the esophagus; it is easily demonstrated by fluoroscopy, although there is little reason to suspect it before this is done. Congenital heart disease in infants is not infrequently associated with malnutrition, because of frequent cough and vomiting, which often result in a difficult feeding problem. In later life the gastrointestinal symptoms of congenital heart disease are much the same as in other forms of heart disease when myocardial insufficiency has developed.

Aneurysm and Mitral Stenosis

Disease of the great vessels, particularly aneurysm, may rarely cause dysphagia. Rheumatic heart disease with mitral stenosis and auricular dilatation may at times produce considerable pressure and displacement of the esophagus, thereby causing noticeable difficulty in swallowing solid food.

Angina Pectoris

The pain of angina pectoris is characteristically substernal, as is the pain of coronary thrombosis; however, both show considerable variation in distribution. Radiation of pain into the jaw and teeth or into the throat is by no means rare. The spread of pain into the epigastrium, below the xiphoid, is comparatively rare but sometimes occurs in patients with a pendulous abdomen. Patients are apt to consider low substernal pain, however, as arising from the stomach. When the pain of coronary thrombosis is associated with gas, nausea or vomiting, or any combination of the three, as is frequently the case, suspicion is naturally directed to the gastrointestinal tract.

The diagnosis of angina pectoris depends entirely on a carefully taken and evaluated history. Generally speaking, the patient notices the following: The pain or discomfort is brought on by effort or emotion. Secondly, the pain may be less severe or absent if he walks when his stomach is empty or aggravated if he walks after eating a heavy meal. The patient thus relates the pain to his digestive tract. The pain may be less severe if the weather is warm or greater if it is cold. The pain may be further aggravated when walking if the patient is emotionally upset. The worst possible combination for the anginal patient, therefore, is cold weather, difficult footing, a full stomach and an upset mind. Thirdly, the patient even while walking often notes a relief of pain by the simple act of belching. This phenomenon is not easily explained, and it is even more difficult to make clear to the patient that his pain originates in the heart and not in the stomach.

Nocturnal pain and gastric distress due to coronary disease may result from overeating. However, it may be a serious sign, often heralding a major coronary infarction.

Nausea is a common accompaniment of coronary occlusion, but I have seen it only once as the major symptom of angina resulting from effort. It appeared and disappeared with substernal and epigastric distress and was readily quieted by nitroglycerin or cessation of effort.

Nausea and vomiting in an elderly patient may be the only sign of coronary thrombosis of the silent type. Much may depend on the patient's interpretation of his low sternal or epigastric discomfort and on whether he calls such discomfort pain. However, one can frequently obtain the usual history of distress by careful questioning. Care must be taken in evaluating nausea and vomiting when other gastrointestinal lesions are present, for example, carcinoma of the stomach, ulcer and gallstones. In these cases, electrocardiograms, especially serial ones, are of decided value. Differentiation of ruptured ulcer or other acute upper abdominal diseases, such as acute pancreatitis, gall-bladder colic or upper intestinal obstruction, is thus made possible. Difficulty arises, however, in cases in which electrocardiographic changes are absent, and a decision concerning exploration must be made. A careful appraisal of the patient's history is most helpful. In spite of all the evidence that can be collected, a decision

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may be impossible and surgery may be undertaken only to reveal a normal abdomen. Fortunately, these cases are infrequent.

Congestive Heart Failure

Acute cardiac decompensation with sudden distention of the liver may also lead one to suspect an acute upper abdominal emergency. However, other clinical signs pointing to a satisfactory diagnosis should be present. The presence of valvular disease, cardiac enlargement, dyspnea and even cyanosis should be striking enough so that an acutely engorged liver is not confused with other upper abdominal lesions.

With insidious congestive failure either from coronary disease or from hypertensive or valvular disease, the gastrointestinal symptoms are less acute and have no constant characteristics. Loss of appetite, gas and vague abdominal distress may result. In these cases, orthopnea may not be so marked, and liver enlargement may be of only moderate degree. Tenderness on palpation of the midepigastrium with resistance there and dullness over Traube's semilunar space should always make one suspect enlargement of the liver. When this is due to congestive failure, the neck veins are almost always engorged, particularly when the patient is in a recumbent position but also discernible when he is upright. This type of failure is often unrecognized in coronary disease. There may be an antecedent history of substernal pain. The physician should be alert to tachycardia and gallop rhythm or a ticktack quality of the heart sounds. A cough may lead one to suspect the heart; in fact, an acute bronchitis with severe coughing may precipitate heart failure. The cough then persists as a 'symptom of pulmonary congestion, and with digestive disturbances the true etiology of the symptoms remains obscure.

When congestive failure reaches the point where ascites is present, bowel function becomes poor, resulting in increasing gaseous distention, anorexia and indigestion.

This whole train of symptoms is also present in chronic passive congestion of the liver associated with ascites caused by chronic valvular disease or constricting pericarditis. Upper abdominal pain after eating may be so severe as to lead one to suspect gall-bladder disease. If congestion can be relieved, the pain may well disappear. In some cases of long standing, hepatic cirrhosis develops, often associated with some degree of jaundice. These patients are difficult to handle and may never be free of gastrointestinal symptoms. Boyer and White¹ have called attention to pain in the right upper quadrant on exertion associated with right-sided heart failure. In my experience, this

has not been encountered commonly, but like many symptoms often unnoticed it may occur more frequently than one suspects.

Embolism

Embolism is one of the most frequently undiagnosed causes of acute gastrointestinal symptoms, and may be pulmonary, renal, splenic, mesenteric or even cerebral. Perhaps the most frequent cause of embolism is rheumatic mitral stenosis, particularly when auricular fibrillation is present. Auricular fibrillation without valvular disease occasionally results in embolism. The mural thrombus of coronary infarction producing embolism may further complicate the gastrointestinal symptoms of this disease. Subacute bacterial endocarditis is another condition in which embolism may occur, as well as the whole train of digestive symptoms that accompany a severe infection. The pain may simulate gall-bladder or renal colic or appendicitis. The sudden onset of severe pain in a known cardiac patient is the keystone of diagnosis, and such a history should make the surgeon suspect the heart. A patient with mitral stenosis and auricular fibrillation should be warned that if such sudden attacks occur, he should immediately consult a physician and suggest the possible cause, thus averting serious and unnecessary operations. Should a diagnosis of mesenteric embolus be made, sufficient time (usually twenty-four to forty-eight hours) should elapse to permit demarcation to take place so that resection will be adequate.

Diaphragmatic Hernia

Certain gastrointestinal lesions frequently cause symptoms that simulate heart disease. Perhaps foremost among these lesions is diaphragmatic or hiatus hernia. This may produce substernal pain extending upward and may be associated with dyspnea, cyanosis and even shock, thus simulating acute coronary infarction. At times morphine must be given to relieve pain. The attacks may be frequent or infrequent. I remember a patient who was supposed to have had two coronary attacks, during which it was difficult or impossible to swallow food or liquid. This gave the clue. Although previous gastrointestinal studies had been done, the hernia was not found until the third examination.

Some of the most incredible complaints from an organic cause seem at first to have no such basis. All physicians tend to ridicule such complaints and classify the patient as being neurotic or as having hallucinations. However, one such case may make one more attentive to bizarre stories. A woman over fifty years of age complained of a loud swishing noise occurring occasionally

after meals and synchronous with her heart beat.² It could be heard ten or fifteen feet away. Examination and fluoroscopy of the heart and chest were negative. Not until some barium was swallowed was a large hiatus hernia discovered. When water and a liberal supply of soda were given, the heart beating against the entrapped portion of the stomach in the chest produced the churning motion of water and gas, thus causing the sound.

Anemia

Diaphragmatic hernia may cause symptoms of coronary disease in another way. Bleeding is not infrequent and marked anemia, with resultant anginal pain and considerable dyspnea on effort, may result. The bleeding may be difficult to control, but once the anemia is gone, the anginal symptoms usually disappear.

Cancer, particularly of the proximal colon, being often the unsuspected cause of anemia, may be another such instigator of cardiac symptoms. Indeed, anemia from any cause may play the same role. Severe congestive failure from anemia alone has been noted on several occasions.

Acute Dilatation of Stomach

Acute dilatation of the stomach after surgical operations may produce so much distress, along with tachycardia, dyspnea and even cyanosis, as to lead one to suspect some pulmonary or cardiac complication. Wise is the man who does not forget the usefulness of the stomach tube. The reverse may also be true,—that is, cardiac failure may cause dilatation of the stomach,—and although this is not common, the stomach tube should be used whenever it is suspected.

Disturbances of Rhythm

Functional cardiac mechanisms, such as paroxysmal auricular fibrillation, flutter and paroxysmal tachycardia, are frequently associated with indigestion. Premature beats, too, are at times a complaint. The latter are likely to be more noticeable during indigestion and are really unrelated to any gastrointestinal disturbance. Every physician has seen patients who had premature beats during examination but who were not conscious of them. Some patients think that paroxysmal auricular fibrillation is precipitated by gastrointestinal upsets, but when it comes to anything specific in the way of quantity or type of food, evidence is lacking. The only precipitating cause that I have encountered and that appears to have some relation is an alcoholic bout, particularly in persons who do not usually drink to excess. The withdrawal of tobacco, coffee and other suspected factors fails to prevent recurrence of these cardiac disturbances.

Many physicians apparently believe there is some relation between gall-bladder disease and functional heart disturbances or coronary disease. The relation between gall-bladder disease and functional heart disturbances is not impressive when viewed critically. However, gall-bladder disease and coronary disease are undoubtedly frequently associated, and the disturbance created by gallstones may aggravate the onset of anginal pain. Possibly the two diseases have a common cause, namely an abnormal deposition of cholesterol.

No precipitating causes of paroxysmal tachycardia have been discovered. In this disorder, as well as in paroxysmal auricular fibrillation or flutter, a sensation of fullness, gas or even nausea may occur during a prolonged attack. Early in life these attacks are well borne unless severe heart damage is present, but in the later years of life such tachycardias may, because of diminishing coronary circulation, produce substernal or high epigastric pain indistinguishable from anginal pain or that of coronary occlusion. Paroxysmal fibrillation is more likely to precipitate failure, not immediately but later, giving rise to the symptoms described under failure.

Symptoms from Treatment

Gastrointestinal symptoms due to treatment may be overlooked or unrecognized. The most important symptoms are those following the use of digitalis. Some patients cannot tolerate digitalis in doses below those that usually produce saturation, namely 1 to 2 gr., or 1 cat unit, per ten pounds of body weight. It is unwise to doubt the patient's statement that such is true. The claims made for various commercial preparations in this regard have little clinical proof. One should not inject intravenously or intramuscularly more than a quarter or a half of a theoretically digitalizing dose unless one is sure that no intolerance exists. Even if no intolerance exists, a calculated dose based on 1 cat unit per ten pounds of body weight should never be given intravenously in one injection but in divided doses not oftener than every three hours. The oral use of Urganin or the oral or the intravenous use of Cedalanid (lanatoside C) may in some cases be less liable to produce toxic symptoms.

Intolerance to such drugs as theobromine and ammonium chloride or even mercurials may prevent their use. Theophylline derivatives, especially theophylline sodium salicylate, seem to produce much less gastric irritation. Attention should be directed to the train of symptoms that may occur from too rapid or too great loss of fluid following diuretics. Two effects may result,

the first from concentration of digitalis bodies in the system, the second from excessive loss of sodium as the result of diuresis. Sudden and obscure deaths may have resulted from the above.

TREATMENT

In the treatment of these gastrointestinal symptoms, as well as of the heart itself, certain procedures should be avoided. Drastic purges are condemned, for although gas and distention may be relieved temporarily, they will recur. It is far better to avoid laxatives and saline cathartics and to rely on a low-roughage diet assisted by enemas of saline solution. A milk diet is suitable for some patients, but generally speaking it fails to keep the patient in a contented frame of mind. In my experience, a soft-solid diet with food that appeals has the advantage. In edema, the diet should have a low salt content, but not when it produces complete anorexia. The same is true for all drugs used. An attempt should be made to keep the patient happy, and to many patients this means a desire for and enjoyment of food. Thirst is often great. A daily fluid intake of 1500 cc. is handled well in most cases; less than this is rarely necessary and may result in an unhappy patient. Any gain in weight in a patient who has had congestive heart failure is almost certain to be caused by fluid, and it is never an encouraging sign.

The bedpan should not be used for cardiac patients, with the exception of those who are al-

most moribund, and then there is little need for it. The commode should be the receptacle of choice. The patient is moved so that his legs hang over the bed, he slides to his feet, pivots to the right or left as the case may be, and then sits down. This procedure can be carried out with a minimum of exertion.

SUMMARY

The gastrointestinal symptoms associated with heart disease are important for two reasons: first, they cause the patient to seek advice regarding his stomach, and secondly, they mislead even the physician. As a result, unnecessary roentgenologic studies may be carried out on a patient who can ill afford to go through such procedures because of his cardiac or financial status. The recognition of the heart condition as the principal cause may save patients from unnecessary and dangerous surgical procedures. Perhaps even more important is the recognition of gastrointestinal lesions causing symptoms of heart disease; to label a patient as having cardiac disease is inexcusable without substantial evidence in both the history and the physical findings. Other causes should be sought, and in such cases a thorough survey is indicated.

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MEDICAL PROGRESS

ORTHOPEDIC SURGERY

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THE problems peculiar to the surgery of trauma have become the focal point of interest of a considerable proportion of medical men, regardless of prewar surgical training. It seems appropriate, therefore, to devote this report of progress in orthopedic surgery to injury and, because of their importance, to the infections with which injury is associated.

TRAUMA AND INFECTION

Infection frequently follows injury and may become of far greater importance than the injury itself. The many and diverse advances made in the field of surgical infection during recent years are often confusing to the clinician and difficult of evaluation. The mechanism by which traumatic infection is produced and develops—in other words, the pattern of infection—varies considerably with the predominant infecting micro-organism. The infection pattern of each of the pathogenic bacteria responsible for these infections is as a rule clearly defined. By it the course of an infection by a given bacterium may be anticipated and appropriate safeguards taken to arrest the local sepsis, prevent complications, and control toxemia. Accurate identification of the infecting bacteria, both aerobic and anaerobic, by culture of the tissue excised at débridement and of the wound exudate is essential to optimum surgical management. Sulfonamide therapy is now recognized as a deterrent to the spread of sepsis, effective through controlling bacterial invasiveness. Antitoxin therapy aids in the control of serious toxemias by neutralizing bacterial toxins absorbed from the septic focus. Increasing attention is being paid to nutritional factors involved in the resistance to infection. Aided by immunotherapy and the bacteriostatic action of the sulfonamides, surgical treatment of the local sepsis is taking broader scope. Earlier drainage of pus is possible, as well as regional division of the septic focus. The immobilization of parts, long recognized as a valuable adjunct, is now placed on a scientific basis. The articles in the

of the best preventives of infection. Reports concerning the results of penicillin and gramicidin are promising, and development of the former in some of the hospitals of the armed forces is being followed with close interest.

Path of Entrance of Bacteria

In general, any injury such as contusion, laceration, compound fracture or an incised or penetrating wound may provide a suitable milieu for bacteria. The local conditions that favor infection are devitalization or necrosis of tissue, diminished blood supply, increased tissue tension resulting from tissue breakdown, hemorrhagic accumulations and foreign bodies—bits of clothing, dirt, shell fragments and so forth. Entrance of bacteria into these areas may be gained through air-borne contamination or direct inoculation, by lymphatic extension from a remote focus, such as a minute crack between the toes in epidermophytosis, or by the hematogenous route. The bacteria introduced by direct inoculation are usually those present on the clothing and skin at the site of injury, although they may be present on the inflicting instrument. The bacteria that are associated with wound infection may, almost without exception, be cultivated from the skin or clothing at various times, the number and type varying with the region injured, with environmental factors and with previous exposure to contamination. Wounds involving the inner recesses of the body, such as the respiratory and gastrointestinal tracts, may, in addition, be inoculated directly with the organisms that make the walls of these systems their natural habitat. All the available evidence points strongly to the conclusion that open wounds are infected by streptococci and staphylococci by subsequent contamination much oftener than by direct inoculation at the time of infliction. Of 355 wounds sustained under various circumstances—that is, industrial, street and miscellaneous accidents—Hare and Willits¹ found no Group A hemolytic streptococci within two hours of infliction, but grew members of this group from 4 of 108 wounds during convalescence under active treatment. The only

which there were coagulase-positive staphylococci, 10 per cent showed a positive culture immediately following infliction, whereas 35 per cent did so during convalescence under treatment.

Contamination of wounds subsequent to infliction and during treatment is the most frequent source of wound infection. The practice of doing frequent dressings of open wounds on surgical wards is to be condemned. The air of these wards usually teems with pathogens introduced from wounds, dressings, bedclothing and the exhalations of other infected patients; from the dressing carriage and the breath and clothing of the attendants; and from the exhalations, skin and clothing of the patient. These organisms, often highly virulent, are blown about with the dust into every quarter of the ward by the constant coming and going of attendants, to settle in profusion upon the exposed wound surfaces. The results are often little short of disastrous. The clear recognition of this pernicious reinfection of wounds has led of late to the general adoption of closed-dressing methods, with incalculable saving in time, life, limb and function, and has eliminated a great deal of futile endeavor. It represents one of the major advances in the surgery of wounds. Open wound dressings should, therefore, be done not on the surgical ward but in a room set aside for the purpose. This room should be as free as possible of atmospheric commotion; adequate masks should be worn by everyone having anything to do with the wound, including the patient, and the dresser's hands should be prepared as for a clean surgical operation. Above these measures, the wound should be closed off from contamination at all other times. It should be exposed for dressing only when absolutely necessary,—for example, when there are signs of toxemia, increasing sepsis or complications, or saturation of the dressing,—and the dressing should then be done with the minimum of disturbance of the healing surfaces. The surgeon should plan at the time of operation to leave the wound in such a condition that only infrequent and nonmanipulative dressings will be necessary. Such a technic is now being stressed widely in civilian and military hospitals.

To the above there is a notable exception, namely, the Carrel-Dakin method of wound management. This superior technic is unfortunately fast becoming a lost art. Where complete facilities are available, and there is a surgical staff adequate in number and training, it undoubtedly has a definite place and will yield brilliant results.

Infecting Organisms

The bacteria commonly responsible for the infections that follow trauma are staphylococci (co-

agulase-positive), hemolytic streptococci, green-producing and nonhemolytic streptococci and clostridia. Anaerobic streptococci, enterococci and gram-negative bacilli (anaerobic) are less frequent wound pathogens. Statistical tables of wound contaminants naturally vary somewhat. In a bacterial analysis of a series of 200 fresh wounds that included lacerations, bullet wounds, dog and human bites, other puncture wounds, compound fractures, traumatic amputation and various automobile and other accidental wounds, Pulaski, Meleney and Spaeth² found the following distribution of organisms: *Staphylococcus aureus*, 52 per cent; hemolytic streptococci, 17 per cent; green-producing and nonhemolytic streptococci, 35 per cent; clostridia, 23 per cent; enterobacteria, 23 per cent; anaerobic nonhemolytic streptococci, 7 per cent; and anaerobic gram-negative bacilli, 2 per cent. The wounds contained on an average three different pathogenic species. This study also revealed that the older was the wound, the more anaerobes were present.

BACTERIOLOGY AND IMMUNOLOGY

A brief résumé of the more recent contributions to the bacteriology and immunology involved in the common types of traumatic infection seems appropriate.

Staphylococci

Identification. Staphylococci are classified at present according to their virulence for man. Strains of *Staph. aureus* are almost without exception pathogenic; those of *Staph. albus* may or may not be. The most reliable test of pathogenicity is the capacity of culture filtrates to coagulate citrated, oxalated or heparinized plasma. Such coagulation is due to a soluble enzymal by-product, staphylocoagulase, common to pathogenic strains (Chapman et al.^{3, 4} and Fairbrother⁵), and is now employed in Army, Navy and most civilian hospitals.

Toxic factors. Staphylococcal pathogenicity depends rather more on the intense local necrotizing action of the bacteria themselves than on their capacity to produce toxins. However, there are several known potent toxins.

Staphylococcal toxin (potent culture filtrate) produces the following clearly demonstrable effects: skin necrosis when injected intradermally, a rapid intravenous lethal action in animals when given in huge doses and hemolysis in animals (probably of minor importance in man). Leukocidin, long associated with filtrate toxin through its destructive or inhibitory action on leukocytes, is still difficult of technical evaluation, although it is thought to be of considerable importance (Blair,⁶ Wright⁷ and Lyons⁸). Hyaluronidase, an enzyme,

the "spreading factor" of Duran-Reynals, has been extracted from cultures of virulent strains. It markedly increases tissue permeability to bacteria (and dyes), intensifies bacterial invasiveness, and enhances infection. It is soluble, stable and non-specific (Duran-Reynals^{9, 10} and McClean¹¹). A separate and distinct toxin, enterotoxin, is associated with staphylococci responsible for outbreaks of food poisoning. In animals its potency when administered intravenously is much greater than that when given orally. In man the symptoms produced are vomiting and diarrhea, abdominal cramping pains and headache. These were symptomatic features in the fatal Bundaberg cases, and Wright⁷ suggests this as the chief lethal factor in distinction to Blair's⁶ idea of the filtrate toxin as the predominant cause of death in this disaster. Lastly, Stevens¹² has reported 3 cases of scarlatiniform rash occurring in *Staph. aureus* infection, implying an uncommon staphylococcal erythrogenic toxin.

Source. Coagulase-staphylococci are normal inhabitants of the human skin and nasal passages. There is evidence that their prevalence on the skin is not so great as is generally believed. Gillespie, Devenish and Cowan¹³ found this group present on the skin of 19 per cent of 159 normal subjects, whereas Smith's¹⁴ finding was 5 per cent of 100 persons. The same investigators found the organisms in the nasal passages of these people in 3 and 32 per cent respectively.

Pattern of infection. From the clinical standpoint, by far the most striking feature commonly seen in staphylococcal infection is the intense local necrotizing action of the organisms. It is as though the tissues in the immediate vicinity had been scorched. Inflammatory fixation is usually prompt, violent and complete, resulting in the formation of simple abscess (less frequently in carbuncle). The lymph channels are blocked with fibrin thrombi, whereby entrance into the lymphatic system is denied to staphylococci or their toxic products. The capillaries thrombose, and the infected area is walled off from the rest of the body (Mentkin). All the evidence points to the assumption that staphylococci gain access to the thrombi formed in the vascular radicles, maintain themselves therein, and from these may enter the blood stream, in fragments detached from the infected thrombus. Expressed in clinical terms, microscopic septic thrombophlebitis may occur in the walls of the abscess. Lyons⁸ has emphasized this fundamental step, as well as the frequency of staphylococci as the responsible organism in the bacteremia that results from it. Conveyed in the blood stream within septic emboli, staphylococci may gain access to various tissues according to a definite pattern that

seems to be governed in part by infarction of the next capillary bed, in part by abscess of the infarcted area and in part by a thrombophlebitis that develops in the metastatic focus. Such metastatic lesions may in turn contribute to the blood stream further embolic contamination, whereby new foci develop. An intermittent bacteremia is thus set up. An abscess developing in an infarct infected with staphylococci may extend to the adjacent tissues or may rupture into a nearby serous cavity to produce a pleural or pericardial empyema.

The lesions that result from and contribute to staphylococcal bacteremia may include any of the following: pulmonary infarction, abscess, pneumonia, pleural empyema and pulmonary thrombophlebitis; visceral infarction and abscess; osteomyelitis; suppurative arthritis; thrombophlebitis of major veins; and brain abscess, thrombophlebitis and meningitis. To this list must be added staphylococcal endocarditis. The mechanism of valvular infection is as yet not defined. It is, however, well known that infected vegetations may become detached, contaminate the blood stream, and cause infarction and so forth. That these lesions comprise those found in metastatic staphylococcal infection is amply supported by autopsy findings. It is not the purpose of this review to discuss the clinical implication of each. The primary focus in these bacteremias may have healed and have been forgotten or may have escaped notice.

Such metastatic lesions vary in size from minute to massive, and may exhibit any part or all of the pattern. Thus, a pulmonary infarction may escape detection or may not occur, yet a positive blood culture attests to the passage of the bacteria through the lungs. On the other hand, infarction may be massive and promptly fatal, or the lesion may suppurate and become fatal later. Variations in local tissue resistance may explain many of these modifications in pattern. However, a suppurative focus in staphylococcal bacteremia is constant. When general infection becomes established, with numerous and extensive metastases and a constant embolic contamination of the blood stream, there is usually a fatal termination.

Exceptions to the above pattern must occur in the nature of things. These are noteworthy but do not alter the validity of the conception. Staphylococci may reverse the usual order and take on some of the attributes of streptococci to produce cellulitis, lymphangitis and a scarlatiniform rash.

Management. The advent of the sulfonamides has not lessened the importance of drainage of staphylococcal pus. The infected area should be exteriorized by adequate drainage, once the inflammation has become fixed locally. In severe infections every effort must be made to improve

the general condition of the patient by sedation and intravenous fluids, and by transfusion, if indicated, while the involved tissues are localizing the infection. Chemotherapy is begun at once. By this means bacterial invasiveness is held in check until natural resistance, aided by appropriate surgical measures, is adequate. Often valuable time may be gained by administering the sulfonamide (except sulfanilamide) intravenously in the form of the sodium salt (prepared capsules). It is essential that the infected part be immobilized by adequate splinting, as discussed later.

In spite of proper and adequate drainage, chemotherapy, splinting and ideal general care, metastatic infection through septic embolism may occur, and vigilance is required to detect intravascular infection at its inception. Such infection may be heralded by a chill, a temperature spike of 103°F. or over and a leukocytosis in excess of 15,000. A sustained high white-cell count, a continued fever, repeatedly positive blood cultures, a palpable thrombosed vein and a pulmonary infarct offer positive evidence of its persistence. Prompt measures directed to control this factor are indicated. Excision of the primary focus when feasible may be successful, or the implicated vein, if accessible, may be excised or ligated.

Once established, metastatic infection must be dealt with according to the same principles employed in the management of the primary focus. Evidence is beginning to appear that penicillin is a highly effective bacteriostatic and bactericidal agent in staphylococcal as well as many other infections. It is not yet available for civilian use.

Efforts to induce staphylococcal immunity in man by antitoxin, toxoid, antibacterial serum, bacteriophage or transfusion have not to date been successful in notably altering the course of infection. Lyons⁸ attributes the improvement claimed for these in reducing the mortality rate in staphylococcal bacteremias to an uncritical selection of cases or to a nonspecific shock reaction enhancing resistance. A true staphylococcal bacteriolysin—excepting possibly penicillin—has not yet been demonstrated.

Aerobic streptococci. The classification of streptococci by serologic methods has relieved much of the confusion that attended the general problem of streptococcal infection and complicated the many questions it raised. Thus the limitations of antibacterial serum therapy can be pointed out, sources of infection can be accurately traced, and the demonstration can be made that any of the various types of streptococci virulent for man may produce a given specific streptococcal clinical picture, such as scarlatina, erysipelas, septic sore throat and so forth. Lancefield, using extracts of

the coccal bodies, has divided the streptococci on the basis of precipitin reactions into thirteen groups—A through M. Each group differs serologically from the others on the basis of a group antigen, C substance, a carbohydrate. Each group is divisible into a number of types on the basis of its capsular material—M substance, a protein—and each includes hemolytic (β), green (α) and nonhemolytic (γ) dissociants. Griffith has derived a similar type classification by using a slide-agglutination technic. Group A (Lancefield) or *Streptococcus pyogenes* (Griffith) is responsible for 95 per cent of serious streptococcal human infections. Group A has been shown to contain at least twenty-nine types. Groups B, C, D, F, G and H may also cause human infection.

Toxic factors (Zinsser,¹⁵ Keefer¹⁶ and Wright⁷). Group A hemolytic streptococci may produce a number of toxic substances. Erythrogenic toxin (A and B), when occurring in large amounts in sensitive persons, gives rise to a scarlatinal rash, fever, vomiting and a rapid pulse. A hemolytic toxin, hemolysin (streptolysin), can be demonstrated, but the part played by this unstable toxin in streptococcal infection is not clear. A fibrinolysin appears to dissolve human fibrin and inhibits its formation from fibrinogen. Both the hemolysin and fibrinolysin are neutralized by streptococcal antitoxin. A leukocidin is also found in streptococcal filtrates that destroy leukocytes in vitro. It is antigenic and type specific. Hyaluronidase (Duran-Reynald's "spreading factor") is present in toxic filtrates.¹¹ It greatly increases tissue permeability and enhances the invasiveness and virulence of the organisms.

Source. Human, Group A, hemolytic streptococci are normal inhabitants of the lymphadenoid tissue of the throat. A considerable proportion of people are carriers of this group. The organism is found in the throat most commonly in winter and the early spring months, particularly in those who have been in contact with patients with acute streptococcal throat infection, especially if they have "colds." Such persons should scrupulously avoid operating rooms and attendance on wounds. It is generally known that Group A streptococci are rarely found on the skin.

Pattern of infection. Infection with hemolytic streptococci (Group A) manifests itself in a variety of ways. Two factors come into play in all these: toxic and septic.

The toxic manifestations are fever, rapid pulse, headache, malaise, prostration or shock, nausea or vomiting and often erythema.

The many clinical septic reactions reveal a considerable similarity. A rapidly spreading cellulitis

(phlegmon) is one of the outstanding characteristics, in sharp contrast with the rapid local fixation (simple abscess) accorded staphylococcal infection. This occurs as a widening area of induration, often erythematous. It marks the progress of the local infection, and is produced by edema, hyperemia, phagocytic cellular infiltration and vascular thrombi. Bacteria may be found throughout. The margins merge abruptly into the normal tissue without early barrier formation. Suppuration may occur and is found in a diffuse thin layer, or it may be more or less localized, as seen in staphylococcal infection. Fixation may not occur for forty-eight hours, during which time the infection may have spread, for example to involve almost the entire thigh or the full length of a limb.

An equally conspicuous characteristic of the streptococcal pattern is the selection by these organisms of certain tissues for their depredations. Such tissues include the following: the lymphatics (and vascular endothelium in general); the fasciae; the cavities with mesodermal epithelial lining, that is, tendon sheaths, joints, bursas and the peritoneum, pleura and pericardium; and the lungs.

The infection of lymphatics may be limited to the local reticular (capillary) portion of the lymphatic system around the wound, producing induration and, if the skin is involved, blushing or erythema. Extension from the lymphatic reticulum may occur into the adjacent tissues, producing cellulitis, with or without suppuration; infection of the reticular lymphatics of the skin in a highly virulent form constitutes erysipelas. Or the main lymph channels may become involved, either directly from a wound more or less appreciably infected or by extension from reticular infection. In the superficial pathways this involvement is revealed by the typical red streaking of lymphangitis; in the deep pathways, the indurated channel may be detected by palpation as a tender cord, especially if grease is applied to the skin to reduce friction (Lyons¹⁷). Extension into adjacent tissues may occur, producing cellulitis and suppuration, and if the intimate anatomic relation of veins and lymphatics is recalled, adjacent phlebitis and thrombophlebitis (Homans¹⁸) is not surprising. Lymph-node infection occurs, with or without appreciable lymph-channel involvement, but the portal of entry is usually readily demonstrable. Suppuration of the nodes may ensue; again, there may be extension into adjacent tissues in the form of cellulitis, with or without suppuration (Frank¹⁹).

Streptococcal infection in a fascial plane may sweep quickly along the deep fascia, usually parallel with the regional body surface, producing a typical cellulitis. Edema may be striking, and may clearly demarcate the limits of the infection. As

the sepsis progresses, erythematous areas may appear and suppuration may develop. The process may be somewhat limited by the fascial compartments. As in most streptococcal invasions, the condition is a grave one, and lymphatic, thrombophlebitic and metastatic complications may arise. The condition may be blood borne following contusion. Hemolytic streptococcal gangrene (Meleny²⁰), termed "gangrenous erysipelas" by the older writers, is essentially a virulent streptococcal cellulitis of the subcutaneous tissues with secondary skin involvement, and leads to massive gangrene. Toxic and septic complications add to the seriousness of the picture.

Infection of tendon sheaths, joints, bursas, pleura and so forth by hemolytic streptococci is frequent and may occur by direct inoculation, by extension from a neighboring focus or via the blood stream. Metastatic joint infection is not uncommon.

Bacteremia occurs when hemolytic streptococci reach the blood stream via the lymphatics, either directly or by extension through thrombophlebitic foci. Clearance is usually prompt unless bacteria continue to pour in. Cardiac valvular lesions may result and in turn provide further contamination from detached vegetations, as in staphylococcal bacteremia. Blood-borne streptococci are prone to metastasize to the lungs,—infarction and bronchopneumonia,—to the joints,—especially in children,—to bone in infants and to the subcutaneous tissues. Metastatic lesions follow the same general pattern of infection as do the primary lesions. They may in turn give rise to further metastases, and if these repeat the process, and infection becomes overwhelming, death finally ensues. A fatal termination may, however, occur with great rapidity in people of subnormal resistance attacked by great numbers of organisms of extremely high virulence.

Streptococci are destroyed in the body by phagocytosis and intracellular digestion, and in this, the macrophage and histiocyte are more effective than the polymorphonuclear leukocyte.

Management. The bacteriostatic action of the sulfonamides has proved to be of enormous value in these infections. By their use time is gained for the patient to marshal the natural forces of resistance and to fix the infection, and for the surgeon to institute most effectively the appropriate measures to improve the general condition and to combat the local sepsis. Complete bed rest in a hospital, sedation, maintenance of body fluids by intravenous saline solution and transfusion, if indicated, are standard general measures. For the local condition, rest by immobilization through appropriate splinting is of the first importance, as discussed below. Hot, moist dressings maintained

over the affected areas are of generally accepted value. Vigilant attention to the local sepsis and alertness to detect complications are essential. In the ordinary form of streptococcal cellulitis—and in erysipelas—surgical drainage should be deferred until suppuration occurs, and should then be restricted to the suppurative zone. In hemolytic streptococcus gangrene, on the contrary, longitudinal incisions are made through the involved tissue and are extended just beyond the margins into healthy tissue as soon as the diagnosis is established. Dakinization of the incisional wounds may then be employed to advantage.

The complications of hemolytic streptococcus sepsis are variously dealt with. Thrombophlebitic foci are blocked off by ligation or excision of the appropriate proximal vein, if it is accessible, and areas of suppuration are drained by incision confined within the suppurative zone. Joint infection is widely treated by repeated aspiration and immobilization; pulmonary, pleural and peritoneal infections are treated by appropriate special local measures.

Streptococcal antitoxin, although it neutralizes the erythrogenic toxin, has a limited therapeutic sphere in surgical infections. It may be helpful in cases in which the signs of intoxication are severe, but it does not alter the septic process. Scarlet fever convalescent serum gives fewer reactions of serum sickness, but it is less potent than the antitoxin. Recently, the purification of antitoxin has considerably lowered the incidence of serum reactions. At present the only method available for supplying specific antibacterial substances in hemolytic streptococcus infections is Lyons's¹⁷ immune-blood transfusion. It aids in clearing the blood stream of organisms and in localizing the infec-

tion, and is applicable to patients with bacteremia. A trained person is required to select the proper donor, that is, one compatible and possessed of sufficient type-specific opsonizing antibody. It has been demonstrated that, at the present time, all commercial antibacterial streptococcal serums are valueless, if not actually harmful.

(To be concluded)

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND SIXTY-SECOND ANNIVERSARY

May 24, 25 and 26, 1943

THE one hundred and sixty-second anniversary of the Massachusetts Medical Society was observed in Boston, on Monday, Tuesday and Wednesday, May 24, 25 and 26, 1943, at the Hotel Statler.

Twelve hundred and seventy-five physicians were registered.

MONDAY, MAY 24

The supervising censors met at 5:00 p.m. in the Hancock Room.

The Cotting Supper was served to 179 councilors in the Salle Moderne. The annual meeting of the Council was held in the Georgian Room at 7:00 p.m. There were 204 councilors in attendance.

TUESDAY, MAY 25

The first general session was opened by the president, Dr. George Leonard Schadt.

Dean Edwin J. Van Etten offered prayer.

Dr. Peirce H. Leavitt and Dr. Leroy E. Parkins acted as chairman and co-chairman respectively. The attendance was 500.

This session took the form of a symposium on burns with special reference to the Cocoanut Grove disaster.

The one hundred and sixty-second annual meeting of the Society was held at 11:00 a.m. in the Georgian Room. Dr. George Leonard Schadt presided. The attendance was 350.

Dr. Schadt spoke at length on the state of the Society. The Annual Oration, "Small Puddles," was delivered by Dr. Edward P. Bagg at the close of the meeting. During the course of the meeting the President introduced Dr. John F. Holmes, of Manchester, delegate from the New Hampshire Medical Society.

The annual luncheon was served in Parlors A, B and C to 151 fellows. Dr. Schadt presided, and Reverend Leo G. Burke, O.M.I., offered grace and benediction.

A clinical meeting was held in the Georgian Room from 2:00 to 5:00 p.m. under the chairmanship and co-chairmanship of Dr. Roger I. Lee and Dr. Dwight O'Hara respectively. The attendance was 550.

In the late afternoon, Mrs. George Leonard Schadt held a tea at the Harvard Club in honor of Mrs. Roger I. Lee and Mrs. Elmer S. Bagnall. Forty ladies were present.

The annual dinner was held in the Georgian Room at 7:00 p.m. with 325 in attendance. Rabbi Samuel J. Abrams said grace.

The speaker at the dinner was Mr. James A. Hamilton, of New Haven, president of the American Hospital Association, professor of hospital administration at Yale University and director of the New Haven Hospital.

Dr. George W. Thorn, Hersey Professor of the Theory and Practice of Physic, Harvard Medical School, and physician-in-chief, Peter Bent Brigham Hospital, delivered the Shattuck Lecture. His subject was "Physiologic Considerations in the Treatment of Nephritis."

WEDNESDAY, MAY 26

There was a general clinical meeting in the Georgian Room from 9:00 a.m. to 12:00 noon under the chairmanship and co-chairmanship of Dr. James W. Manary and Dr. Edward J. O'Brien, Jr., respectively. The attendance was 550.

From 12:00 noon until 2:00 p.m. there was a series of section meetings and luncheons.

The Section of Medicine held forth in Parlors B and C under the chairmanship of Dr. Laurence D. Chapin. The attendance was 44.

The Section of Surgery met in Parlor A, under the chairmanship of Dr. Oliver Cope. The attendance was 40.

The Section of Pediatrics met at the Junior League, Zero Marlboro Street, under the chairmanship of Dr. James M. Baty. The attendance was 33.

The Section of Obstetrics and Gynecology met at the Women's Educational and Industrial Union, 264 Boylston Street, under the chairmanship of Dr. Christopher J. Duncan. The attendance was 51.

The Section of Radiology met in Room 404, Hotel Statler, under the chairmanship of Dr. Joseph H. Marks. The attendance was 22.

The Section of Physiotherapy met in Parlors D and E, Hotel Statler, under the chairmanship of Dr. Henry A. Taddell. The attendance was 20.

The Section of Dermatology and Syphilology met in the Hancock Room, Hotel Statler, under the chairmanship of Dr. J. Harper Blaisdell. The attendance was 36.

From 2:00 to 5:00 p.m. a general clinical meeting was held in the Georgian Room under the chairmanship and co-chairmanship of Dr. Charles E. Mongan and Dr. Frank R. Ober, respectively. The attendance was 450.

There were 63 technical and 16 scientific exhibits.

The motion pictures attracted the attention of a large number of fellows.

The lists of admissions and deaths are appended, together with the official lists of officers, standing and special committees, councilors, censors and so forth.

MICHAEL A. TIGHE, *Secretary*

ANNUAL MEETING OF THE SOCIETY

The one hundred and sixty-second annual meeting of the Massachusetts Medical Society was called to order by the president, Dr. George Leonard Schadt, in the Georgian Room of the Hotel Statler in Boston at 11:00 a.m., May 25, 1943. There were approximately 350 fellows present.

The Secretary offered the record of the last annual meeting as published in the *New England Journal of Medicine*, issue of July 9, 1942, and moved its adoption. This motion was seconded by a fellow, and it was so ordered by vote of the Society.

Dr. Schadt presented Dr. John F. Holmes representative of the New Hampshire Medical Society. Dr. Holmes responded as follows:

I am very pleased to be here with you today, and I congratulate the Society on the wonderful program that has been presented this morning and the program that has been arranged for the rest of the meeting. It is a pleasure to be here, and I feel highly honored.

No delegates were listed from Maine, Vermont, Rhode Island or Connecticut. It was explained by the Secretary that these states were not represented owing to the exigencies of the War.

The Secretary announced that the membership of the Massachusetts Medical Society, as of May 26, 1942, was 5708, that the Society has gained during the current year 136 new members and 17 restorations, that it has lost 76 members by death, 16 by resignation and 16 by deprivation of their membership. He added that the net gain has been 45 and that the membership as of May 25, 1943, was 5753.

At the request of the President, the members stood for one minute in silent tribute to the memory of those fellows who had gone beyond.

At that point Dr. Peirce H. Leavitt, vice-president, assumed the chair. Dr. Schadt addressed the Society as follows:

Since our last meeting we have lost a valuable and honored servant of the Massachusetts Medical Society in the person of Dr. Charles Shorey Butler. Dr. Butler had been treasurer of the Massachusetts Medical Society, I believe, since 1931, approximately twelve years. He gave a great deal of himself to the Society, which he loved dearly. After many years of faithful service, he continued in office when the requirements of his health should have demanded a rest. He was finally prevailed on to ask for an indefinite leave of absence, which was granted. Dr. Butler died February 23, after an illness of several months. He had a peaceful death, and one that ended much suffering.

It was my privilege to know Dr. Butler intimately and to love him. He was a most kind and able man, one of the gentlemen of the old school, who, unfortunately, are passing from this scene.

At the request of Dr. Schadt the members stood for one minute in silent tribute to the memory of Dr. Butler.

It was moved and seconded that the President appoint a committee to bring in suitable resolutions on the death of Dr. Butler. It was so ordered by vote of the members.

The Secretary asked the district secretaries to aid his office in gathering the list of fellows who have entered and who will enter the service of our Country. Dr. Schadt seconded this request and called on the district presidents to help in this effort.

Dr. George L. Schadt delivered the presidential address on the state of the Society. He spoke as follows:

It is a pleasant duty for each president retiring from office to submit at the annual meeting a report on the state of the Society. This I shall do now.

I am very much pleased to be able to tell you that the state of the Massachusetts Medical Society at the present moment is excellent. This I hasten to assure you is not due to anything I have done, but due entirely to the unselfish work of the other officers, particularly Dr. Peirce H. Leavitt, vice president, Dr. Michael A. Tighe, secretary, and Dr. Eliot Hubbard, Jr., acting treasurer, and of course to the chairmen and the members of the various standing committees and the appointed committees during the year. I have learned anew—and it has been a very refreshing thought, too,—that when one wishes anything done one should ask a busy man. He will always have time to do it. I have asked many busy doctors during the year to accept appointments on committees as chairmen and as members, to carry out difficult and tedious assignments, and I am happy to say I did not have one refusal.

As has already been stated, the Massachusetts Medical Society is in excellent condition, both physically and

financially. Starting my year as your president, it was with the determination that we should have a peaceful, constructive year—a year free from petty and unprofitable squabbles. I think I am correct in saying that in the past we have had some petty squabbles and have always found them unprofitable. Your president has enjoyed the duties of his office very much. He has had the very happy privilege of making fifteen official visits to fourteen of the eighteen district medical societies. During these visits he has had the privilege and pleasure of meeting many of the members, and he hopes that he has made friends among them. It is a delightful experience to visit the different district societies, to talk with the officers and the members, and to learn the problems they have,—and it may be said these problems vary in the different sections of the State. Many of these problems, too, are local ones, and should be handled locally, and your president wishes to say that he has discovered that these problems are being handled in an excellent manner.

In going about among the various district societies, I have endeavored to tell the members what the Massachusetts Medical Society is doing, what some of the problems are that have arisen, to answer any questions the members may have, and also to gain the good will and support of the membership as a whole.

The late Dr. Burrage, our very efficient secretary for many years, wrote a most interesting and instructive history of the Massachusetts Medical Society, bringing it up, I believe, to 1926. Dr. Burrage left a number of volumes to the Society, requesting the secretary to present to each president during his term of office a copy of the book. Dr. Tighe presented me with my copy, and may I say I have read it from cover to cover and enjoyed it tremendously. I urge the members of the Society to read this history of the oldest medical society in the United States in point of uninterrupted meetings from the time of its beginning, in 1781, to the one hundred and sixty-second anniversary, in 1943. I cannot refrain in leaving this subject from expressing the hope that some historically minded member of the Society will carry on this history from the point where Dr. Burrage left off,—the year 1926,—bringing the history up to date.

May I now extend my heartfelt thanks and appreciation to all the officers with whom I have worked during the year and to all committee chairmen and committee members. I shall always have the deepest appreciation for what they accomplished for me during the year. It is not my purpose to mention many names in this report, but I do not believe the report would be complete without speaking of several.

The interest and the work of Dr. Michael A. Tighe, our secretary, is deserving of the gratitude of every member of the Society—a grand gentleman and a born secretary. Frankly, I find it difficult to understand how it would have been possible to have carried on without him. He knows every detail of what is going on in the Society, and his good advice and his assistance are always readily available. I wish at this time to extend to him my affectionate regard and my thanks for his help during this year.

May I also express to Dr. Eliot Hubbard, Jr., our acting treasurer, my deep appreciation for his help during this rather trying year. Dr. Hubbard stepped into the breach when our late treasurer, Dr. Charles S. Butler, found it impossible to continue with his duties, because of his health. Dr. Hubbard rather reluctantly assumed the office of acting treasurer. He gave unselfishly of his time

to the work, and on Dr. Butler's death took over all the duties of the office. Dr. Hubbard has steered the financial ship of state most capably, and though we shall all miss Dr. Butler, for whom I am sure we all had a great affection, we may feel that in Dr. Hubbard we have a worthy successor.

Dr. Charles Shorey Butler, the treasurer of the Massachusetts Medical Society since June 9, 1931, passed away on February 23, 1943. Dr. Butler served the Society as treasurer for approximately twelve years. His devotion to the Massachusetts Medical Society was complete. He gave unselfishly of his time and of himself in guarding its financial resources. He spent much time investigating investments that would make secure the principal. He was a lovable man—a man of whom it may well be said,—paraphrasing a remark by Oscar Wilde,—“... a charming gentleman, he had no enemies; he had many friends, and everyone loved him.” It was my privilege to know Dr. Butler intimately, and knowing him was to love him. He most reluctantly and only after much urging relinquished his duties, and then only when the state of his health made any other step impossible. In the death of Dr. Butler the Massachusetts Medical Society has lost a rare personality, an ideal treasurer and a friend.

The Society, as already stated, is in sound condition. It is strong, vigorous, virile. During the year it has conducted much constructive work, of which more will be said later. The Society has grown in membership, and as will be noted from the figures given herewith—we have increased in membership steadily in the last five years:

June 8, 1939	5438
May 22, 1940	5542
May 22, 1941	5639
May 26, 1942	5708
May 18, 1943	5752

These figures, of course, include members now in the armed services, but members nevertheless of the Massachusetts Medical Society. It seems to me the outstanding feature of these figures is the fact that during this tremendous cataclysmic war the Society has grown.

You will be interested, I am sure, to know—and I received these figures from Dr. Reginald Fitz, of Suffolk, at a recent meeting of the State Committee of the Procurement and Assignment Service—that according to the records of the *American Medical Directory* there were 8085 physicians in Massachusetts in 1942. Of this number 2734 were not members of the Society, and of this group 1269 are in the armed services. On the other hand, 5351 were members of the Massachusetts Medical Society. You will note an apparent discrepancy between these figures and the figures I have given you above, but since the directory is published only every other year there is, naturally, a lag in the figures. With reference to the number of members of the Society in the armed forces, I am informed that to date there is a total of 1256. Thus, a total of 2525 doctors from Massachusetts are members of the armed services—the Army, the Navy, the Marine Corps and the Public Health Service.

I am glad to say that the Council meetings held during the year have been well attended. There is one fly in the ointment, however: although many councilors attend the morning session, far too many leave at the intermission or directly after the Cotting Luncheon. As a matter of fact, there have been a number of occasions in past years and during this year that at the afternoon meeting

there has barely been a quorum, so that business might be transacted. As you and I know, the Council is the deliberative body of the Massachusetts Medical Society, its membership is based on the premise that every councilor represents twenty members of the district from which he comes. Therefore, when a councilor does not attend a Council meeting or attends only part of the meeting twenty members have no representation what ever or have only partial representation. In my opinion the districts should be most careful in the selection of their councilors electing those gentlemen who realize the importance of the position and will give up the three days necessary to come to Boston and to attend the Council meetings from beginning to end. It might just as well be said here that some of the councilors living in Boston and towns adjacent not only do not attend the Council meetings, but when they do attend leave at noon or shortly thereafter. This problem has been discussed at the Executive Committee meetings, and at the annual meeting of the Council it was moved and voted that the meetings in the future begin at 10 in the morning and continue without interruption to 2 in the afternoon, or until all business is transacted. I am sure that following this rule we shall have a quorum of the Council at every session.

The Committee on Membership has been most active and has done a splendid job. During 1942 and 1943 it received a total of 95 membership applications of which 65 were approved, 11 were disapproved, 9 were disapproved by the district committees, and 16 were held for further information. It is most interesting to note that there was close agreement between the central committee and the district committees in that there was only a difference of two in the number disapproved by these committees.

The Committee on Membership has recommended to the Executive Committee that the question of establishing a junior membership in the Massachusetts Medical Society be postponed for the time being. The question whether the Society should establish a junior membership was brought to the attention of Dr. Tighe, our secretary during the year. We discussed the question and then brought it to the attention of the Executive Committee which recommended that it be passed on to the Committee on Membership. It may be that at some time in the future junior memberships will develop into a worthwhile project in the Society.

The State Committee of the Procurement and Assignment Service has done an excellent piece of work under difficult and trying conditions. It was my privilege to sit in at most of the meetings, and I was also asked to go to Washington on a number of occasions to attend meetings presided over by Dr. Frank Lahey, chairman of the Directing Board of the Procurement and Assignment Service. These committee meetings were very much worth while. I am informed by Dr. Lahey, in a letter dated April 24, 1943, that approximately 2300 doctors from Massachusetts are in the armed forces, of whom 1200 are members of the Massachusetts Medical Society and 1100 are not. Again it should be mentioned that there is an apparent discrepancy between these figures and some figures given earlier in the report. The discrepancy is apparent only because the figures were arrived at on different dates and under different circumstances. The quota for Massachusetts in 1943—and I have seen these figures recently—is 33 per cent complete up to April 27. Five hundred and ninety more physicians will be needed from Massachusetts before the end of the year, and the majority of these physicians will have to be

taken from the large centers that is from the large districts—Suffolk, Middlesex, South, Norfolk, and other districts in and about Boston, Massachusetts, together with New York and Connecticut has the unenviable reputation of being one of the three states that have not filled their quotas for 1942, the percentage being 90 per cent. It is not necessary for me to tell you of the urgent need for physicians in the armed services. In going about the State and in visiting Washington, Chicago and other cities I have heard all the arguments pro and con. I have heard arguments about essentiality, until frankly I am fed up with the word. In my opinion, the word essential is the cause of more trouble in procuring the adequate number of physicians than any other one word or one thing, and I for one should like to see the whole question of essentiality ruled out. In my opinion it would be a very constructive thing and would help immeasurably in getting many physicians to enter the services who now are hesitating for one reason or another. If every doctor of service age, that is under forty five or fifty, could be put in uniform on active service.

The Committee on Ethics and Discipline has had a busy year and under its very able chairman has done a fine piece of work. Your president has had the privilege of attending all its meetings. It is somewhat discouraging to listen to some of the problems that are brought up to this committee and to realize that there are men practicing our profession who apparently are not guided by the principle announced many years ago.

Do unto others as you would have them do unto you. Some of the cases presented have demonstrated a sordid viewpoint and greed, and others lack of appreciation of the ethics of medicine under which we practice in this enlightened age in the State of Massachusetts. May we hope that as the years go on there will be less and less of this in our profession, and less and less need for problems of this kind being brought before this committee.

In speaking of the Treasurer's report, may I again express to Dr. Hubbard our newly elected treasurer, my deep appreciation for his help during this trying year. Dr. Hubbard informs me that our finances are in excellent condition. We have, I believe approximately \$270,000 in bonds. Why the Society has this much money I do not know, and have never been able to find out to my satisfaction. It is my distinct impression that this money should be at work doing good deeds in the way of scholarships or in some other manner that the proper committee might well deem desirable. Dr. Hubbard further informs me that to date he has collected \$41,493 in dues but that there are still 706 members whose dues remain unpaid totaling \$7060. When this amount is received our treasurer will have collected \$48,553. I am quite sure that when the second bill goes out the members who have not paid will promptly do so. They will then receive the *New England Journal of Medicine* and will know that they are pulling their weight in the boat.

The *Journal* has continued its successful career under the able and brilliant editorship of a gentleman whose name you well know and under the direction of a very able committee. You will I am sure, be interested in the figures given herewith, showing the increase from year to year of subscriptions to the *Journal*, in 1943 totaling 10,347.

SUBSCRIBERS	1943	1942	1941	1940	1939
M. M. S.	4,071	4,740	4,873	4,844	—
Regist.	4,494	3,781	3,168	2,693	2,305
Student	1,551	696	—	—	—
Totals	10,347	8,717	8,041	7,542	6,355

This includes an order on May 1 for 541 subscriptions from the Surgeon General's Office, for distribution to all Army hospital installations of 25 beds or more.

During 1942, the *Journal* received 1984 new "outside" subscriptions, a total that is over 50 per cent greater than the total received in 1941. Of these subscriptions, 1085 were from regular subscribers and 899 from medical students. As would be expected there were many cancellations, undoubtedly owing to enlistment in the armed forces; the net increases were 216 regular subscribers and 711 medical students, which total 927. (As of December 31, 1942, journals were being sent to 5083 members of the Society (a decrease of 74 from the 1941 figure), 3462 regular subscribers and 1193 medical students, a total of 9738, which is greater by 853 than the total for 1941. This does not include 348 members of the New Hampshire Medical Society, who receive the *Journal* once a month.

The editorial board took action on 238 manuscripts during 1942, a decrease of 90 compared with the figure for 1941. Of these papers, 169, or 71 per cent, were accepted.

Operations for the year resulted in a net loss of \$17,550, which is approximately \$2450 less than the amount appropriated by the Society. The net amount received from the Society was \$19,100 the balance, approximately \$1550, being covered by an increase in current assets. The net cost per member of the Society was \$3.43, as compared with \$3.20 in 1941.

There was an increase in operating expenses due to the larger circulation, the increased cost of binding and mailing and the fact that in 1942 fifty-three issues of the *Journal* were distributed, which happens every seven years when January 1st falls on a Thursday.

It is difficult to predict what will happen in 1943. Undoubtedly the number of member subscribers will be decreased owing to their enlistment in the armed forces; on the other hand, it seems likely that the number of "outside" subscribers will hold its own or possibly show a slight increase in spite of cancellations. Expenses should decrease as a result of lower publication costs (provided the total circulation is smaller) and an increase in advertising revenue, owing to higher rates, which became effective on January 1. The decrease in the number of manuscripts submitted for publication may become a serious problem. In any event, the pagination of the *Journal* will be cut down since the members of the editorial board believe that the high standards for acceptance should not be lowered.

I am sure you will all agree with me that we may take deep satisfaction in having an exceptionally excellent journal, one that ranks very high throughout the Country.

As most of you already know, the Society has within recent years been carrying on under a budget system. The Committee on Finance, the chairman of which has given unselfishly of his time on this work, has prepared within recent years a very complete budget, and the Society has been living within this budget. Anyone who has had any experience at all in preparing budgets and living within them knows the difficulties that develop. However, I may say that we are living within our budget, and that notwithstanding a decrease in revenue due to members leaving for the armed services.

Within recent years there have developed within the Society several district-society journals. At present there

are three: one published by the Worcester District Medical Society; one published by the Norfolk District Medical Society; and one published by the Hampden District Medical Society. It is my studied opinion that the development of district medical society journals is a good thing for the Society, provided their activities are restricted to the district society that they represent. It is well, certainly, for the larger district societies that there be some medium through which the news of the district may be transmitted to its members from time to time: what the members are doing, what the hospitals in the district are doing or may have to offer in the way of clinics to the membership, and any other items that may be of local interest. I do not believe, however, that these journals should have a circulation larger than its membership. I am of the opinion that if and when the circulation of a district journal goes beyond that of its membership, then we may well look for and expect difficulties of one kind or another. Certainly these journals should not expect to compete with the *New England Journal of Medicine*, our own journal. Whereas the latter covers a much larger and a more comprehensive field, the former should, as already noted, devote their efforts to the county societies. I am rather hopeful that some of the larger district societies will see fit to publish journals, and it seems to me, too, that two, three or four adjacent smaller districts might well co-operate in publishing a journal that would cover their respective districts.

As I have gone about the State visiting the various district medical societies, I have taken the opportunity of pointing out the fact that the Massachusetts Medical Society as constituted today is practically completely decentralized, in that the Society is in the hands of its members, and not in the hands of any group in or about any of the districts or in or about Boston. Today we have three large state-wide committees. These committees have a duly elected member from each of the eighteen district societies. Besides this, the officers are all members *ex-officio*. These committees, as you know, are the Executive Committee of the Council, the Committee on Public Relations and the newly organized Committee on Legislation. The work of each is important, and having attended practically all the meetings of these three committees this year, I can assure you that much constructive work was done in behalf of the Society.

I should like to emphasize at this time a point I have made in talks to the various districts. It is this: any member of the Massachusetts Medical Society may at any time gain a hearing in the Council by bringing to the attention of one of the councilors from his district the subject he wishes discussed. His subject will be received and considered. If found worth while it will be accepted. In other words, I wish to re-emphasize the fact that the Massachusetts Medical Society today is a society of approximately 6000 doctors, and is, as Abraham Lincoln so well said: "A government of the people, for the people and by the people."

With reference to the Executive Committee of the Council, this committee has worked hard all year, and since the amount of work crossing Dr. Tighe's desk is increasing each year, the subjects and problems to be considered are many and diversified. This committee as originally planned and set up was organized to lessen the detail of work brought before the Council and to shorten the Council meetings. Unfortunately this desired re-

sult has not been achieved as yet, but we are quite sure that it will be in the years to come.

The Committee on Public Relations has held regular meetings and has discussed many very important problems—problems with which you are all familiar, I am sure. One of the most important of these, of course, was the work of a subcommittee meeting with Mrs Emma Tossant, chairman of the Industrial Accident Board. As the result of these co-operative meetings, considerable constructive work has been achieved in bringing about a better approach to the care of the injured workman, and a more equitable treatment of the doctor on the individual case.

The Committee on Legislation is the last of these large committees organized—as a matter of fact, it was only organized this year, but has already done a splendid bit of work. I am happy to be able to report that without lessening the scope of its work, this committee was able to return to the treasurer \$1450 of its budget.

We are ending this year under a new set of by laws. The committee delegated to revise the by laws did an excellent piece of constructive work, and although we all did not see eye to eye with them, I am happy to say that the by laws have worked out well and with practically no confusion. One of the outstanding changes was that the collection of dues was placed in the office of the treasurer of the Society, instead of through the treasurers of the district societies. This collection of dues has worked out quite satisfactorily, and I am certain that in the years to come all the wrinkles will be smoothed out. It has, of course, meant a lot of work for the treasurer and his office, but he has done a splendid job and deserves much credit. As stated elsewhere in this report there are still 706 members who as yet have not paid their dues. I am quite sure, however, this has merely been an oversight and that soon all their dues will have been received.

We have had several new committees that have done excellent work. One of these is the Committee on Industrial Health. This committee, under the able chairmanship of one of our most distinguished members, has carried out an extremely constructive program. The committee has held two large meetings, both at the Harvard Club, one in November and the other the latter part of April. Both these meetings were well attended—the first having an attendance of around 300, and the latter 160. Both programs were excellent. One of the most gratifying features of these meetings was the caliber of the speakers and how very ready each of these distinguished gentlemen was to accept the committee's invitation to appear on the program and to bring to the members of the Society up-to-date viewpoints on the various problems of industrial health. This committee will, of course, continue its work, and I believe plans in the future to hold a meeting in Springfield, and probably in other cities in the Commonwealth.

As you know, because of war conditions, it was found necessary to postpone the New England Postgraduate Assembly for the duration. This is very much regretted but, of course, cannot be helped. Another necessity was the transference of the annual meeting this year from Springfield, where it was scheduled to be held, back to Boston. However, your officers and the Committee on Arrangements felt that under the circumstances, because of gasoline restrictions and the probability that we would be able to entertain a larger number of doctors in Boston than in Springfield, this was desirable.

Another new committee that has performed an outstanding service is the Military Postgraduate Committee, organized the latter part of last year. This committee developed as the result of the simultaneous appreciation on the part of three of our members of the need for the Society of developing some plan of service for the various Army camps and hospitals, as well as Navy hospitals. There seemed to be a definite necessity for assisting the personnel of the camps, hospitals and stations to obtain speakers and to develop worthwhile programs. The committee was organized in November, and since that time twenty-seven instructors have given thirty-two lectures at various Army installations and one at a Navy station. At a meeting of this committee the other evening, a gentleman representing the Navy voiced their appreciation of the advantages of this plan, and stated that they are going to adopt it and extend it throughout the Navy organization in the coming years.

This work has, of course, been carried on only by the Massachusetts Medical Society this year, but we believe that all the New England states should join in the program, since in practically all of them there are Army and Navy hospitals and stations that need assistance of this kind. Then too, the University of Vermont College of Medicine is situated in Burlington, the Yale University School of Medicine in New Haven, and I believe a two-year course is given by Dartmouth at Hanover. It should be a rather simple procedure to unite the New England states in this work. At the annual meeting of the Council last night, a motion was passed authorizing the Military Postgraduate Committee to continue its work and to get in touch with the other state societies through their secretaries, and our Society for the coming year was authorized to subsidize the expense of the program up to \$500.

Another new and important committee is the War Participation Committee, this committee having been organized within the last two weeks. Its personnel consists of a progressive group of our members, and the committee has an excellent chairman. I am sure it will do some grand work during the war and for some years after the war is over.

Among other new activities of the Society that have developed during the year I now mention the action of the Council at its meeting last evening in adopting a resolution authorizing the officers of the Society to take over more space in the Boston Medical Library. I for one firmly believe that our home is and should be in the Boston Medical Library, since in my opinion these two organizations should work shoulder to shoulder. Situated as it is in the Fenway and so centrally located, it is easy of access from any part of Boston. As I have stated, the Society will very shortly take over more space. In view of several progressive movements now on foot, there is no question that the Society will use the present space and add space much more in the future than it ever has in the past. Plans are in progress for developing a medical service bureau, similar to the bureau maintained at the New York Academy of Medicine. This bureau will and should be the center of medical information in the City of Boston, having on record every day what is going on in the various hospitals and what medical meetings are taking place—in other words, making available up-to-the-minute information to any member of the Society or to any doctor concerning what is going on in and about Boston that will interest him. You will have more information on this project from time to time.

Another important resolution that was offered, voted on and accepted was the plan to establish a Postwar Loan

Fund. This subject was submitted to the Council by your president as follows:

The subject I am going to discuss with you is something that has been in my mind all year long, but it seemed to me that I should wait until the annual meeting of the Council before bringing it out. I shall present the plan I have in mind and shall ask Dr. Roger I. Lee, the incoming president, to exercise his prerogatives in appointing a committee.

The last war, as you know, was a comparatively short war. Many of us had been in practice five, ten or fifteen years when we went away. I happened to be in service for twenty-two months; some of us were in for ten, twelve or fourteen months—I believe the average was fourteen months. We got back into practice quickly. Some of us were lucky and had little trouble, but a lot of the men had difficulty getting started. I know because I talked with a great many of them. They needed a car, or they needed an office.

I can think of the story of one man, let's call him Bill Smith, who came back and was quite a hero. He had been wounded severely and was brought home, and when he came back he met John Jones, a banker, who thought Bill Smith was a wonderful hero and told him what a fine fellow he was. And then he said to Bill Smith, "What can I do for you?" Bill replied, "I should like to see if I can borrow a little money." The banker said, "Of course you can. I'll be glad to give it to you. How much do you want?" "Twelve hundred dollars." "By the way, what about collateral?" John Jones asked. Bill Smith said, "This will be only for a year." However, the banker looked at him with a cold eye and said, "If you haven't any collateral I can't let you borrow the money." That was poor Bill Smith's position. He was a great hero, he had fought for his country in the war and he had been wounded, but he never got the \$1200—at least not from the banker.

A lot of men came back wounded and could not return to the type of practice they had engaged in before. They would have liked very much to have gone into something like refraction, but they did not have the money and they could not do it. As the result of the war many men lost out, not because of their service, but because of the fact they could not afford to rehabilitate themselves.

I think we have a great opportunity in the Massachusetts Medical Society today. This war is different. It is a long war. It has already lasted, so far as we are concerned, nearly a year and a half. It is going to last another two or three anyway. Our friends have gone, men who have been in practice five, ten or fifteen years. Many of those men are coming back wounded or in ill health. A surgeon may never be able to operate again. An internist may never be able to do that type of work. If he could do refraction or skin work, if he could get started with six or ten months' headway, it would be a great thing for him. A great many coming back are going to need special treatment until their wounds and their nerves are healed, and a majority of them are coming back without collateral.

My plan—and I have talked it over with a few men in the Society—is one to develop a fund in the Massachusetts Medical Society. Call it the Postwar

Loan Fund. Let it run something on the order of the Morris Plan, any member of the Society being able, without embarrassment and without collateral, to make application for a loan. That application is endorsed by one or two members of the Society. The amount would be limited, and each application would receive careful consideration. Such a scheme could be easily put into effect. To come to us rather than to an otherwise affable banker, or to a loan shark, would save our friends and our colleagues a tremendous amount of embarrassment.

I can visualize a man coming home and wanting to go to Harvard or Boston University or Tufts for postgraduate study. Incidentally, possibly the medical schools might be willing to cut the fee in half or cut it out entirely for the ex-service man. The amount to be borrowed might be \$1000 or \$1500. That can be decided. The time in which the loan has to be repaid might run one or two years. That, too, would be decided by a committee.

I can visualize further. I can see men who are not coming back, who are leaving wives, and children who need to be educated. There are quite a number of paths this plan might follow.

You say, "Well, where are you going to get the money?" I think the preliminary fund could be obtained by assessing every member of the Massachusetts Medical Society who had not had the privilege of serving with the armed forces, because of age, disability or another reason, \$10, with the opportunity of contributing more if he so desired. I think we could easily get \$50,000 to start with, and if we needed more we have a backlog of over \$200,000. Why does the Massachusetts Medical Society need \$200,000 in bonds? That is something which has been a source of worry to me all year long. We have done nothing with it. It has just been invested. There must be something constructive we can do with the money instead of having it lie in our treasury.

A resolution was made, seconded, and accepted that the incoming President appoint a committee known as the Postwar Loan Fund Committee. This committee's duties will be to study every phase of this problem, to submit a report of progress at the meetings of the Council in October and in February, and to submit a final report at the annual meeting of the Council in May, 1944. You will, of course, be kept informed through your councilors with reference to this subject, and at the annual meeting next year have the final report of the committee.

As previously stated, the work of many other committees, standing and special, has been excellent and deserves the deepest appreciation of every member of the Massachusetts Medical Society. The reports of these committees will be incorporated in the report of the annual meeting of the Council, held on Monday evening, May 24, so that I feel it is unnecessary to mention them at this time, with the exception that I wish again to express to the chairmen and to the members of every committee in the Society my profound feeling of obligation and deepest appreciation for what they have done for me and for the Society during this rather trying year.

I have purposely held to the end of this report certain remarks with reference to the Medical Service Corporation, better known to you as the Blue Shield. You are all familiar, I am sure, with the fact that the Blue Shield

was inaugurated by the Massachusetts Medical Society, and was developed through the very excellent work of Dr Thomas H Lanman and Dr James C McCann. Dr Lanman gave unselfishly of his time in obtaining from the Legislature the enabling act permitting us to organize this corporation. On his induction into the Army, it was necessary for him to relinquish the work, which was taken up by Dr McCann and carried on so efficiently. May I say at this point that it is impossible for me to adequately express my appreciation of the work of Dr Lanman, and my admiration for the work of Dr McCann in developing the Blue Shield and getting it where it is today. Dr McCann has given tirelessly of his time and his talents, and the Massachusetts Medical Society will ever be indebted to him. It was my pleasure and privilege to make many trips with Dr McCann to various parts of the country to study the different plans, and to determine the plan that would in the opinion of Dr McCann and his committee, work most efficiently in the Commonwealth of Massachusetts.

The Blue Shield began to function just about a year ago. The Blue Shield, gentlemen in my opinion is a success, and as time goes on will be a greater success with each coming year. As a matter of fact I am convinced that the Blue Shield will be one of the most successful projects the Massachusetts Medical Society has ever initiated and carried through. It is quite true that it has been a bit slow in getting under way, but this has been due to many factors beyond the control of the Blue Shield. One of the important reasons was the entrance of this country into the war, another, the development of multiple taxes including the Victory tax. In my opinion by far the most important reason—and I say this with considerable diffidence and understanding—is that up to the present time the members of the Massachusetts Medical Society have on the whole not given the Blue Shield the united and loyal support that it should and must have. Unfortunately, many members have apparently made no effort to understand what the Blue Shield stands for and many of these gentlemen have criticized the Blue Shield and made statements they otherwise would not have made had they heard the clear exposition presented in practically every district medical society by Dr McCann and had they taken the time to read the several pamphlets sent to them and the articles appearing in the *New England Journal of Medicine*. It is my hope that in the ensuing year the members who have criticized and have not given their support to the Blue Shield will learn to understand it and will get back of it wholeheartedly. Only in this way will it be possible to make it the success that it should be.

At the present time there are forty groups enrolled in the Blue Shield, the total number of persons enrolled is 2329 with a total of 1170 contracts. Thirty three hundred doctors have signed up as participating physicians but again may I say that unfortunately not all this number have taken the time or given the effort to understand what the Blue Shield is and what it will do for the individual and for them if given a fair trial. Frankly it was our hope at this time last year that we would have approximately 3000 persons enrolled in the Blue Shield. As stated we have 2329. With your support and cooperation we can, I believe, next year have 10,000 or more persons enrolled in the Blue Shield. May I earnestly beseech your understanding support of the Blue Shield. I am sure that if there is any question that is not clear

to any of you, merely writing to Dr McCann, or if you wish writing to me, will bring you a prompt answer and clarification of the problem.

In concluding this report on the state of the Society, may I express to the members of the Massachusetts Medical Society the realization on my part of the great honor it has done me in permitting me to serve as president of the Society for the last year. I can assure you that I have kept the interest of the Massachusetts Medical Society paramount at all times and that I have done my best to see that the Society was conducted in a dignified manner during the year.

And finally, I should like to leave with you a message that I have left with all the district societies that it has been my privilege to visit. It seems to me that a short quotation from a poem by Allan McIntosh, a young Scot who died in the last war, is most appropriate at this time—when all the world is in turmoil when we are all concerned about our loved ones and doing everything possible to bring about a quick victory and a lasting peace. Of the former, there is no question for in my opinion victory is only a matter of time and lasting peace a problem that we must and can solve. Allan McIntosh's lines appear on a very beautiful monument in Edinburgh—a memorial to the Scots who died in World War I. In his relief below the lines are shown Scottish pipers marching to war their pipes playing their scarfs blowing in the wind and back of them the soldiers and back of them the artisans followed by the wives the sweethearts and the children. Above this bas-relief appear these inspiring lines—lines gentlemen that I beg you to make your own as they are and have been mine for many years.

If it be life that waits I shall live forever
unconquered

If death I shall die at last strong in my
pride—and free

Dr Schadt was greeted with loud applause at the close of his masterly address, which showed a wide knowledge of the problems facing the Society.

Dr Schadt assumed the chair and introduced the annual orator, Dr Edward P. Baggs, of Holyoke, chief medical evacuation officer of Region II and president of the staff of the Holyoke Hospital. Dr Schadt called attention to the title of the oration—"Small Puddles." He wanted the members to understand that even though Dr Baggs was a pediatrician and therefore might be expected to know a good deal about small puddles the reference in the title had nothing to do with Dr Baggs' chosen field of endeavor.

The oration, which was published in the May 2 issue of the *New England Journal of Medicine* was beautifully and scholarly done and Dr Baggs was loudly applauded at its conclusion.

Dr Schadt introduced Dr Roger I. Lee, president for the ensuing year, Dr Elmer S. Bagnall, president-elect, Dr Eliot Hubbard, Jr., treasurer and Dr Michael A. Tighe, secretary. They all re-

sponded fittingly and expressed their pleasure at their enlarged opportunities to serve.

Dr. Frank R. Ober moved that the meeting adjourn. This motion was seconded by a member, and it was so voted.

Dr. Schadt declared the one hundred and sixty-second annual meeting of the Massachusetts Medical Society adjourned at 12:30 p.m.

MICHAEL A. TIGHE, *Secretary*

APPENDIX

ADMISSIONS RECORDED FROM MAY 26, 1942, TO MAY 25, 1943

YEAR OF ADMISSION	NAME AND RESIDENCE	MEDICAL SCHOOL
1942	*Abkowitz, Herbert, Everett	Kansas City University of Physicians and Surgeons
1942	*Adelman, Ernest Bernard, Bridgewater	Middlesex
1942	Albertowicz, Theodore John, Lowell	Tufts
1943	Allers, Olga Eleanore, Wellesley	Woman's Medical College of Pennsylvania
1942	Andreson, Lawrence Helmar, West Somerville	Tufts
1943	Angelo, Peter John, Quincy	Tufts
1942	Aranson, Albert, Newton Centre	Boston University
1942	*Argoff, Joseph, Fitchburg	Missouri College of Medicine and Science
1943	Avery, Bennett Franklin, Brookline	University of Michigan
1942	Baptista, Jesse, Fall River	Tufts
1943	*Berger, John Jacob, West Concord	Middlesex
1942	Berry, Franklyn Doane, New Bedford	Boston University
1942	*Bluestein, Jacob Kenneth, Bardsville	Middlesex
1942	*Boeh, Louis S., Conway	Middlesex
1943	Boyd, James Gelston, Westborough	Boston University
1942	Brady, Frank William, Lowell	Tufts
1942	*Brahm, Leo, Worcester	Friedrich Wilhelm University of Berlin
1942	*Buoniconto, Pasquale, Hathorne	Royal University of Naples
1942	Burger, Franklyn Donaldson, Wellesley Hills	University of Michigan
1943	*Burns, Francis Albert, Foxboro	Middlesex
1942	Chace, John Frederick, Hudson	Tufts
1942	Clauser, William Joseph, Boston	Indiana University
1942	Cole, William Gregory, Pittsfield	Columbia University
1942	†Cook, William Wilder, Quincy	Tufts
1942	*Cooperstein, Harry Joshua, Fall River	Middlesex
1942	*Corrado, John Charles, East Boston	Middlesex
1942	Cosgrove, James Francis, Jr., Worcester	Tufts
1942	*Cottone, Peter Paul, Marlboro	Middlesex
1942	Cox, Robert Downing, Worcester	Tufts
1942	Crowell, Lois Blanche, Tewksbury	Boston University
1943	Currier, Wilber Dale, Brookline	University of Nebraska
1942	Curry, John James, Boston	Tufts
1942	Desmet, George William, North Andover	Tufts
1942	*Devine, Joseph William, Boston	College of Physicians and Surgeons, Boston
1942	*Donovan, William Francis, Watertown	Middlesex
1942	*Eames, Thomas Harrison, Arlington	College of Physicians and Surgeons, Boston
1943	Elliot, Howard Lailey, Brookline	McGill
1943	Epstein, Ida Florence, Roxbury	New York Medical College and Flower Hospital
1942	*Erbe, Henry Herman, Otis	Middlesex
1942	Fadgen, John Francis, Clinton	Loyola University
1942	Fanger, Herbert, Salem	New York Medical College and Flower Hospital
1942	*Ferrante, Anthony, Allston	College of Physicians and Surgeons, Boston
1942	Forsley, Richard, Lowell	Tufts
1942	Frank, Howard Alvin, Boston	New York University
1943	Gettings, Thomas Lawrence, Fall River	Tufts
1942	*Giallombardo, Nicholas Perrone, Somerville	Middlesex
1942	Gidman, Francis Thomas, Boston	Tufts
1942	Glass, Sarah Elizabeth, Worcester	Rush Medical College
1942	*Goglia, Alfred Anthony, Taunton	College of Physicians and Surgeons, Boston

1943	*Goldman, Harold Sumner, Medford Middlesex
1942	*Goldstein, Morris, Cambridge	Middlesex
1942	Goodman, Doris Ryan, Natick	Tufts
1942	*Gordon, George Samuel, Lynn	...Middlesex
1943	*Gordon, Robert Knott, Winthrop	Middlesex
1942	Grandfield, Robert Edward, West Roxbury	Harvard
1942	Grandmont, Irene Olive, Foxboro	Boston University
1942	*Grzyb, Henry Andrew, Southbridge	College of Physicians and Surgeons, Boston
1942	Hardy, Erving Douglas, Worcester	Tufts
1942	Harken, Dwight Emory, Cambridge	Harvard
1942	Hayes, John Joseph, Jr., Brighton	Georgetown
1943	Hertig, Arthur Tremain, Newton Highlands	Harvard
1943	Hindle, William Vincent, Boston	Harvard
1943	*Hobica, Norman, Allston	Middlesex
1943	Howley, Edward Joseph, East Weymouth	Tufts
1943	Ingersoll, Francis McCall, Boston	Harvard
1942	Johnson, Carl Cordes, Brighton	Harvard
1942	*Johnson, Harry Taylor, Waltham	Middlesex
1943	Johnson, Walfred, Worcester	George Washington University
1942	*Kenney, John Aloysius, Mansfield	Midwest Medical School
1942	*Kenny, Donald Ellsworth, Medford	Middlesex
1942	Klam, Najeb, Boston	Boston University
1943	Klemperer, Friedrich Wilhelm, Lexington	Harvard
1943	Liebman, Sumner David, Boston	Harvard
1942	*Lunauro, Ulysses David, Lynn	Middlesex
1942	Loofbourow, Dorothea Gano, Cambridge	University of Cincinnati
1942	*Lowenberg, Benjamin, Dorchester	University of Lausanne
1942	MacMahon, Harold Edward, Cambridge	University of Western Ontario
1943	Mankowich, Ralph, Waltham	Boston University
1943	*Manning Ralph A., Winchester	Middlesex
1943	McKell, David McCandless, Jr., Brookline	Harvard
1942	Miller, Edward Alexander, Sagamore	Boston University
1942	*Morrin, Harry Joseph, Roxbury	Middlesex
1942	*Nadelman, Benjamin Isidore, Roxbury	Middlesex
1942	Ober, Robert Emil, Cambridge	Tufts
1942	Olken, Harry George, Cambridge	Tufts
1942	Olshausen, Kenneth Wolfgang, Boston	University of California
1942	Porter, Reno Russell, Pepperell	Medical College of Virginia
1942	Potter, Theodore Alexander, West Newton	Boston University
1942	Quigley, George Edward, Newton	Boston University
1942	Rea, Stanley Leroy, Westfield	Stanford University
1943	Rice, Theodore Adams, Worcester	Harvard
1943	Richards, Anthony, Tewksbury	Tufts
1942	Rubin, Abraham Louis, Fort Devens	Tufts
1942	Rutledge, David Ivan, Wellesley Hills	University of Nebraska
1942	Ryan, William Francis, Palmer	Tufts
1942	*Sandler, Samuel, Cambridge	Middlesex
1942	Saward, Ernest Welfton, Waltham	University of Rochester
1943	*Schiller, Louis, F	City University of Physicians and Surgeons
1942	†Schott, Norbert A	of Physicians and Surgeons, Boston
1942	*Schwartz, Frank	of Physicians and Surgeons, Boston
1943	*Schwartz, Leo, Springfield	Middlesex
1943	Seligman, Arnold Max, Brookline	Harvard
1943	*Shalett, Irving Joseph, Brookline	Middlesex
1943	*Sherman, David Edward, Springfield	Middlesex
1942	Shipp, Luther Murry, Medford	Tufts
1943	Silveus, Esther, Boston	University of Pittsburgh
1942	Sise, Herbert Stanwood, Brookline	Harvard
1942	Skinner, David, Newton Centre	Harvard
1942	*Smith, Leonard, Westfield	Middlesex
1943	*Solomon, Alex, Adams	Middlesex
1942	Sostek, Samuel Bertram, Medford	Boston University
1943	*Souza, Charles Marshall, Dighton	Middlesex
1942	*Sprinz, Helmuth, Boston	University of Berlin
1943	Stowell, Joseph May, Chestnut Hill	Tufts
1943	Sutor, Douglas Gilman, Springfield	Tufts
1942	Sullivan, Arthur James, Fall River	Jefferson Medical College
1942	*Sullivan, Francis Robert, Jamaica Plain	Middlesex

1943	Sullivan, Robert Edward, Dorchester.....	Tufts
1942	Taddeo, Arthur E., Natick.....	Tufts
1943	Tansey, Joseph Logan, Jamaica Plain.....	Harvard
1943	*Thannhauser, Siegfried Josef, Brookline.....	University of Munich
1942	Thorn, George Widmer, Cambridge.....	University of Buffalo
1942	*Tucci, John Hugh, Dorchester.....	Middlesex
1942	Tucker, Charles Albert, Boston.....	Tufts
1942	*Venti, Matthew, Methuen.....	Middlesex
1943	*Wallace, Thomas Edmund, Revere.....	Middlesex
1942	Waugh, Richey Laughlin, Brighton.....	University of Minnesota
1942	*Weinert, Thaddeus Conrad, Cambridge.....	Middlesex
1942	Williams, Conger, Milton.....	McGill
1942	Williams, John Webster, Newton.....	George Washington University
1942	*Wiseblatt, Aaron Carl, Dorchester.....	Middlesex
1942	*Wojcicki, Henry Telesfor, Fall River.....	Middlesex
1942	*Wyant, John Anderson, Fitchburg.....	College of Physicians and Surgeons, Boston
1942	Yasuna, Elton Ralph, Worcester.....	New York University
1943	Young, Edward Lorraine, III, Cambridge.....	Harvard
1943	*Zarella, Anthony George, Medford.....	Middlesex

Total number of new fellows admitted . . . 136

*The candidate, after a personal interview, was approved by the Committee on Membership and permitted to take an examination before a board of censors.

†Deceased.

DEATHS REPORTED FROM MAY 26, 1942, TO MAY 25, 1943

ADMITTED	NAME	PLACE OF DEATH	DATE OF DEATH	AGE
1906	Adams, Charles Waldron.....	Cambridge	October 20, 1942.....	63
1895	†Ash, John Henry.....	Quincy	February 15, 1943.....	73
1899 } 1921 }	Bailey, William Thomas.....	Boston	January 16, 1943.....	74
1898	Blakely, David Newton.....	Brookline	October 15, 1942.....	75
1913	Bowen, Enos Emanuel.....	East Boston	July 15, 1942.....	60
1886	Brackett, Elliott Gray.....	Boston	December 28, 1942.....	82
1893	Briggs, Charles Albert.....	Assonet	December 14, 1942.....	79
1893	Bryant, Alice Gertrude.....	Boston	July 25, 1942.....	80
1899	Butler, Charles Shorey.....	Boston	February 23, 1943.....	72
1916	Butler, Francis Joseph.....	Worcester	June 7, 1942.....	59
1895	†Byrne, Charles Armstrong.....	Hatfield	April 3, 1943.....	80
1913	Carvell, Hanford.....	Lanesville	February 15, 1943.....	67
1891	†Chapin, Delia Lucretia.....	Springfield	October 7, 1942.....	88
1898	†Cochran, William James.....	Somerville	August 29, 1942.....	80
1942	Cook, William Wilder.....	Quincy	January 23, 1943.....	56
1913	Cox, Stanley Cullen.....	Holyoke	June 7, 1942.....	58
1906	Dana, Harold Ward.....	Brookline	May 8, 1943.....	65
1906 } 1923 }	Deems, Oren Manfred.....	Springfield	April 17, 1943.....	63
1896	Dennison, Archibald Sayre.....	Lynn	January 22, 1943.....	73
1881	Dixon, Robert Brewer.....	Boston	December 16, 1942.....	86
1899	Dow, David Crooker.....	Cambridge	May 27, 1942.....	67
1926	Dressler, Morris Lawrence.....	Fort Dix, New Jersey	May 6, 1943.....	54
1922	Dwyer, Philip Roche.....	Salem	February 28, 1943.....	49
1900	Easton, Elwood Tracy.....	Boston	January 31, 1943.....	67
1899	†Ellsworth, Samuel Walker.....	Quincy	November 27, 1942.....	72
1907	Faxon, William Otis.....	Stoughton	November 12, 1942.....	89
1911	French, Ralph Winward.....	Fall River	December 7, 1942.....	59
1895	†Gates, Ernest A.....	Springfield	January 4, 1943.....	73
1926	Goldman, Harry.....	Roxbury	April 22, 1943.....	47
1888	Greenwood, Allen.....	Boston	October 23, 1942.....	76
1899	Handy, Harry Tucker.....	Scituate Center	October 8, 1942.....	68
1875 } 1921 }	†Harding, Edward Mitchell.....	Newton	December 19, 1942.....	90
1895	†Harris, Arthur Eugene.....	Lynn	July 11, 1942.....	72
1907	Henderson, Charles Russell.....	Reading	March 31, 1943.....	75

1903	Hickey, John Joseph	Peabody	January 17, 1943	75
1920	Hogan, Daniel John	Roslindale	August 15, 1942	55
1895	†Holmes, Mary Salona	Worcester	April 4, 1943	72
1897	†Jack, Edwin Everett	Brookline	November 16, 1942	79
1897	Jackson, Oliver Howard	Fall River	June 1, 1942	70
1915	Jacoby, Rudolph	Boston	August 20, 1942	52
1917	Jewett, Howard Wakefield	Lowell	March 18, 1943	63
1891	†Jenkins, Frank Louville	Lynn	April 21, 1943	90
1890	†Kaan, George Warton	Shirton	April 14, 1943	88
1907 } 1927 }	†Kazanjyan, Hampar Paul	Los Angeles	September 20, 1942	70
1932	Keeley, Thomas Henry	Monson	August 28, 1942	48
1892	†La Marche, Walter Joseph	Cambridge	May 30, 1942	80
1939	Laurin, Theophile	Lowell	April 10, 1943	72
1927	Leonard, Edward Joseph	Dorchester	February 15, 1943	41
1905	Lowell, William Holbrook	Winchester	March 31, 1943	67
1920	Lucy, John Joseph	Boston	December 28, 1942	47
1927	Luther, Eliot Horton	Westfield	May 2, 1943	47
1935	Maguire, James Alfred	Atlantic	May 31, 1942	36
1902 } 1939 }	Mahony, Francis Ronan	Lowell	May 17, 1943	64
1903	Malone, Charles	Jamaica Plain	October 10, 1942	67
1902	McBain, William Hearst	Malden	May 9, 1942	68
1933	McGuinness, John Francis	Woburn	June 17, 1942	49
1929	Metzger, Armand Oliva	Chicopee	July 1, 1942	52
1910	Miller, George Fremont	Belfast, Maine	March 22, 1943	67
1898	†Morse, Almon Gardner	Hingham	July 27, 1942	74
1928	Olef, Isadore	Dorchester	December 16, 1942	45
1889 } 1941 }	Peterson, Reuben	Duxbury	November 25, 1942	80
1910	Phillbrick, Roscoe Hunter	New Orleans, Louisiana	Unknown	62
1911	Popoff, Constantine	Hampton Beach, New Hampshire	May 30, 1942	58
1901	Priest, Herbert Bancroft	Ayer	March 12, 1943	68
1926	†Rice, George Brackett	Brookline	March 28, 1943	83
1907	Robbins, Eugene Stanley	West Palm Beach, Florida	January 18, 1943	70
1942	Schott, Norbert A	Boston	March 25, 1943	40
1897	Shultz, Frederick Charles	Leominster	June 23, 1942	69
1902	Stack, Charles Francis	Hyde Park	April 3, 1942	71
1892	Stuckney, Edwin Pangman	Arlington	January 8, 1943	80
1909	Stone, Thomas Newcomb	Haverhill	April 21, 1943	63
1913	Temple, William Franklin	Boston	December 25, 1942	55
1937	Thau, William	Gap Military Res., Pennsylvania	February 14, 1943	46
1908	Walker, Harry		October 30, 1942	61
1899	†Walsh, Charles		September 6, 1942	83
1914	Willoughby, Earle Carlisle	North Reading	June 23, 1942	60

†Retired fellow

Total number of deaths of active fellows	59
Total number of deaths of retired fellows	17
Grand total	76

OFFICERS FOR 1943-1944

PRESIDENT	Roger I Lee, Boston, 264 Beacon Street
PRESIDENT ELECT	Elmer S Bagnall, Groveland, 281 Main Street
VICE PRESIDENT	Daniel B Reardon, Quincy, 1186 Hancock Street
SECRETARY	Michael A Tighe, Lowell Office, Boston, 8 Fenway
TREASURER	Eliot Hubbard, Jr, Cambridge, 29 Highland Street
ASSISTANT TREASURER	Norman A Welch West Roxbury Office, Boston, 570 Commonwealth Avenue

ORATOR Joseph C Aub, Boston, Massachusetts General Hospital

COMMITTEES ELECTED BY THE DISTRICTS

EXECUTIVE COMMITTEE OF THE COUNCIL — Established 1941 (Members <i>ex-officio</i> and one councilor and alternate elected by the councilors of each district medical society)	
PRESIDENT	Roger I Lee, Boston, 264 Beacon Street
PRESIDENT ELECT	Elmer S Bagnall, Groveland, 281 Main Street
VICE PRESIDENT	Daniel B Reardon, Quincy, 1186 Hancock Street

SECRETARY: Michael A. Tighe, Lowell. Office, Boston, 8 Fenway.
 TREASURER: Eliot Hubbard, Jr., Cambridge, 29 Highland Street.

Term Expires 1944

BERKSHIRE: Not yet elected.
 FRANKLIN: Frederick J. Barnard, Greenfield, 479 Main Street. (Alternate: William J. Pelletier, Turners Falls, 113 Avenue A.)
 HAMPDEN: George L. Steele, Springfield, 20 Maple Street. (Alternate: Edward A. Knowlton, Holyoke, 207 Elm Street.)
 MIDDLESEX NORTH: William M. Collins, Lowell, 174 Central Street.
 NORFOLK: Carl Bearse, Boston, 483 Beacon Street.
 WORCESTER NORTH: C. Bertram Gay, Fitchburg, 62 Day Street. (Alternate: Francis A. Reynolds, Athol, 43 Cottage Street.)

Term Expires 1945

ESSEX SOUTH: Loring Grimes, Swampscott, 84 Humphrey Street. (Alternate: Charles L. Curtis, Salem, 10 Federal Street.)
 HAMPSHIRE: L. Beverly Pond, Easthampton, 115 Main Street. (Alternate: Joseph D. Collins, Northampton, 187 Main Street.)
 MIDDLESEX SOUTH: Dwight O'Hara, Waltham. Office, Boston, 416 Huntington Avenue. (Alternate: Sumner H. Remick, Waltham, 735 Trapelo Road.)
 NORFOLK SOUTH: Daniel B. Reardon, Quincy, 1186 Hancock Street. (Alternate: Henry A. Robinson, Hingham, 205 North Street.)
 SUFFOLK: Donald Munro, Boston, 818 Harrison Avenue. (Alternate: Charles C. Lund, Boston, 319 Longwood Avenue.)
 WORCESTER: Ralph S. Perkins, Worcester, 10 Hackfeld Road. (Alternate: Gordon Berry, Worcester, 36 Pleasant Street.)

Term Expires 1946

BARNSTABLE: Not yet elected.
 BRISTOL NORTH: William H. Allen, Mansfield, 70 North Main Street. (Alternate: Ralph M. Chambers, Taunton, Taunton State Hospital.)
 BRISTOL SOUTH: Not yet elected.
 ESSEX NORTH: Frank W. Snow, Newburyport, 24 Essex Street. (Alternate: Rolf C. Norris, Methuen, 247 Broadway.)
 MIDDLESEX EAST: Edward M. Halligan, Reading, 37 Salem Street. (Alternate: Richard Dutton, Wakefield, 33 Avon Street.)
 PLYMOUTH: Peirce H. Leavitt, Brockton, 129 West Elm Street. (Alternate: Charles D. McCann, Brockton, 12 Cottage Street.)

Committee on Public Relations—Established 1931 (One councilor elected yearly by each district medical society; the president and president-elect of the Society are chairman and vice-chairman, respectively, and the vice-president and secretary of the Society are members *ex-officio*).

BARNSTABLE: W. D. Kinney, Osterville.
 BERKSHIRE: P. J. Sullivan, Dalton, 471 Main Street.
 BRISTOL NORTH: J. H. Brewster, Attleboro, 178 South Main Street.
 BRISTOL SOUTH: H. E. Perry, New Bedford, 159 Cottage Street.
 ESSEX NORTH: E. S. Bagnall, Groveland, 281 Main Street (secretary of committee).
 ESSEX SOUTH: Loring Grimes, Swampscott, 84 Humphrey Street.
 FRANKLIN: W. J. Pelletier, Turners Falls, 113 Avenue A.
 HAMPDEN: P. E. Gear, Holyoke, 188 Chestnut Street.
 HAMPSHIRE: A. J. Bonneville, Hatfield, 60 Main Street.
 MIDDLESEX EAST: J. H. Blaisdell, Winchester. Office, Boston, 45 Bay State Road.
 MIDDLESEX NORTH: D. J. Ellison, Lowell, 8 Merrimack Street.
 MIDDLESEX SOUTH: J. P. Nelligan, Cambridge, 2336 Massachusetts Avenue.
 NORFOLK: N. A. Welch, West Roxbury. Office, Boston, 520 Commonwealth Avenue.
 NORFOLK SOUTH: F. A. Bartlett, Wollaston, 308 Beale Street.
 PLYMOUTH: C. D. McCann, Brockton, 12 Cottage Street.
 SUFFOLK: A. A. Hornor, Boston, 319 Longwood Avenue.
 WORCESTER: J. M. Fallon, Worcester, 390 Main Street.
 WORCESTER NORTH: J. G. Simmons, Fitchburg, 30 Myrtle Avenue.

Committee on Legislation—Established 1942 (One councilor elected yearly by each district medical society).

BARNSTABLE: Not yet elected.
 BERKSHIRE: P. J. Sullivan, Dalton, 471 Main Street.
 BRISTOL NORTH: J. L. Murphy, Taunton, 23 Cedar Street.
 BRISTOL SOUTH: Not yet elected.
 ESSEX NORTH: E. H. Ganley, Methuen, 251 Broadway.
 ESSEX SOUTH: C. A. Worthen, Lynn, 19 Park Street.
 FRANKLIN: H. M. Kemp, Greenfield, 42 Franklin Street.
 HAMPDEN: W. A. R. Chapin, Springfield, 121 Chestnut Street.
 HAMPSHIRE: A. N. Ball, Northampton, Northampton State Hospital.
 MIDDLESEX EAST: J. M. Wilcox, Woburn, 6 Bennett Street.
 MIDDLESEX NORTH: W. H. Sherman, Lowell, 9 Central Street.
 MIDDLESEX SOUTH: B. F. Conley, Malden, 51 Main Street (chairman of committee).
 NORFOLK: J. C. V. Fisher, West Roxbury. Office, Boston, 510 Commonwealth Avenue.
 NORFOLK SOUTH: D. L. Belding, Hingham. Office, Boston, 80 East Concord Street.
 PLYMOUTH: J. J. McNamara, Brockton, 231 Main Street (interim appointment).
 SUFFOLK: W. B. Breed, Boston, 264 Beacon Street.
 WORCESTER: L. M. Felton, Worcester, 36 Pleasant Street (secretary of committee).
 WORCESTER NORTH: F. A. Reynolds, Athol, 43 Cottage Street.

Committee on Nominations—Established 1874 (One councilor and alternate elected yearly by each district medical society)

BARNSTABLE W D Kinney, Osterville (Alternate P M Butterfield, Harwich)

BRANFORD P J Sullivan, Dalton, 471 Main Street (Alternate, C F Fasce, Pittsfield, 311 North Street)

BRISTOL NORTH W H Allen, Mansfield, 70 North Main Street (Alternate J L Murphy, Taunton, 23 Cedar Street)

BRISTOL SOUTH E F Cody, New Bedford, 105 South 6th Street. (Alternate R B Butler, Fall River, 278 North Main Street)

ESSEX NORTH G L Richardson, Haverhill, 94 Emerson Street (Alternate R C Norris, Methuen, 247 Broadway)

ESSEX SOUTH D S Clark, Salem, 2 Oliver Street (Alternate P P Johnson, Beverly, 1 Monument Square)

FRANKLIN F J Barnard, Greenfield, 479 Main Street (Alternate W J Pelletier, Turners Falls, 113 Avenue A)

HAMPDEN A G Rice, Springfield, 146 Chestnut Street (Alternate E P Bagg, Holyoke, 207 Elm Street)

HAMPSHIRE L B Pond, Easthampton, 115 Main Street (Alternate J D Collins, Northampton, 187 Main Street)

MIDDLESEX EAST R R Stratton, Melrose, 538 Lynn Fells Parkway (Alternate E M Halligan, Reading, 37 Salem Street)

MIDDLESEX NORTH M A Tighe, Lowell, 9 Central Street (Alternate W H Sherman, Lowell, 9 Central Street)

MIDDLESEX SOUTH Dwight O'Hara, Waltham Office Boston, 416 Huntington Avenue (Alternate J C Merriam, Framingham, 198 Union Avenue)

NORFOLK D D Scannell, Jamaica Plain Office, Boston 475 Commonwealth Avenue (Alternate H J Inglis, Chestnut Hill Office, Boston, 43 Bay State Road)

NORFOLK SOUTH D B Reardon, Quincy, 1186 Hancock Street (Alternate H A Robinson, Hingham, 205 North Street)

PLYMOUTH W H Pulsifer, Whitman 26 Park Avenue (Alternate P H Leavitt, Brockton, 129 West Elm Street)

SUFFOLK W B Breed, Boston, 264 Beacon Street (Alternate A A Hornor, Boston, 319 Longwood Avenue)

WORCESTER R P Watkins, Worcester, 332 Main Street. (Alternate W F Lynch, Worcester, 390 Main Street.)

WORCESTER NORTH B P Sweeney, Leominster, 5 Gardner Place (Alternate G P Kenney, Fitchburg, 62 Fox Street)

STANDING COMMITTEES FOR 1943-1944

ELECTED BY THE COUNCIL, MAY 24, 1943

Date of Appointment

PUBLICATIONS—Established 1825

R M Smith June 6, 1933 (appointed chairman May 21, 1941)

J P O'Hare June 9, 1936

Conrad Wesselhoeft June 2, 1937

W B Breed February 7, 1940
Oliver Cope May 21, 1941

ARRANGEMENTS—Established 1849

G M Morrison May 21, 1941 (appointed chairman June 24, 1942)
R J Heffernan May 25, 1942
S C Wiggan June 24, 1942
R I Smith June 24, 1942
G G Bailey November 13, 1942

ETHICS AND DISCIPLINE—Established 1871

R R Stratton June 9, 1936 (appointed chairman May 21, 1941)
W J Brickley February 3, 1937
A G Rice June 1, 1938
F R Jouett May 21, 1940
A R Gardner May 21, 1941

MEDICAL EDUCATION—Established 1881

R T Monroe May 21, 1941 (appointed chairman February 4, 1942)
G D Henderson June 1, 1938
C S Keefer February 4, 1942
I R Jankelson May 25, 1942
A W Allen May 24, 1943

MEMBERSHIP—Established 1897

H F Newton June 9, 1931 (appointed chairman May 25, 1942)
John E. Fish June 17, 1930
P H Leavitt June 1, 1938
A W Reggio May 21, 1940
S H Remick May 24, 1943
W H Allen, H Q Gallupe, A E Parkhurst
— representing the Supervising Censors

PUBLIC HEALTH—Established 1912

F P Denny June 1, 1938 (appointed chairman June 7, 1939)
G N Hoeffel June 17, 1930
H L Lombard June 4, 1935
H F Day June 7, 1939
F W Marlow, Jr May 25, 1942

MEDICAL DEFENSE—Established 1927

A W Allen June 7, 1927 (appointed chairman June 7, 1939)
E D Gardner June 7, 1927
W R Morrison June 9, 1936
(*sec pro tem*)
Horatio Rogers June 7, 1939
I M Dixon August 17, 1942

SOCIETY HEADQUARTERS—Established 1932

W H Robey February 24, 1937 (chairman)
C G Mixer June 8, 1932
E C Miller June 4, 1935
G L Schadt May 24, 1943
M A Tighe May 24, 1943

FINANCE—Established 1938

F C Hall July 8, 1943 (chairman)
(interim appointment)
E L Hunt June 2, 1938
C F Wilinsky June 2, 1938
E J O'Brien, Jr June 2, 1938
P P Johnson October 4, 1939

INDUSTRIAL HEALTH — Established 1942.

Dwight O'Hara May 25, 1942
(chairman)

J. C. Aub May 25, 1942
D. L. Lynch May 25, 1942
H. C. Marble May 25, 1942
T. L. Shipman May 25, 1942
J. N. Shirley May 25, 1942
F. N. Manley May 24, 1943

SPECIAL COMMITTEES

CANCER — Established 1917.

E. L. Hunt, *chairman*; F. G. Balch, E. M. Daland,
P. E. Truesdale, C. C. Simmons.

REPRESENTATIVES TO THE MASSACHUSETTS CENTRAL HEALTH COUNCIL

BARNSTABLE: W. D. Kinney
BERKSHIRE: R. J. Carpenter
HAMPTON: G. D. Henderson
NORFOLK: F. P. Denny
SUFFOLK: R. B. Osgood
WORCESTER: E. C. Miller

PUBLIC EDUCATION (a subcommittee of the Committee on Public Health) — Established 1930.

F. P. Denny, *Chairman*; G. N. Hoeffel, *secretary*;
G. R. Minot, W. H. Robey, E. H. Place, C. C.
Simmons, J. H. Pratt, H. W. Stevens, J. B. Ayer,
H. P. Mosher (interim appointment), F. R. Ober,
E. P. Joslin, J. D. Barney, H. L. Lombard, Joseph
Garland.

POSTGRADUATE INSTRUCTION — Established 1932.

Reginald Fitz, *chairman*; L. E. Parkins, *secretary*;
J. W. O'Connor, R. N. Nye, C. J. Kickham.

PHYSICAL THERAPY — Established 1935.

A. L. Watkins, *chairman*; F. P. Lowty, R. B. Osgood.

COMMITTEE TO CONSIDER EXPERT TESTIMONY — Established 1936.

F. R. Ober, *chairman*; David Cheever, F. P. McCarthy,
Carl Bearse, W. J. Brickley.

COMMITTEE ON AUTOMOBILE INSURANCE CLAIMS — Established 1937.

H. C. Marble, *chairman*; H. M. Landesman, *secretary*;
P. P. Henson.

COMMITTEE ON CONVALESCENT CARE — Established 1938.

T. D. Jones, *chairman*; H. E. Gallup.

COMMITTEE TO STUDY THE PRACTICE OF MEDICINE BY UNREGISTERED PERSONS — Established 1939.

Richard Dutton, *chairman*; B. F. Conley, E. F. Timmins.

TWENTY-FIVE VOTING MEMBERS IN MASSACHUSETTS HOSPITAL SERVICE, INC. — Established 1939.

B. H. Alton, E. S. Bagnall, G. M. Balboni, W. B.
Breed, L. D. Chapin, H. F. Day, J. F. Donaldson,
A. W. Dudley, John Fallon, J. E. Flynn, A. R.
Gardner, H. W. Godfrey, J. H. Lambert, A. A.
Levi, J. C. Merriam (interim appointment), Don-
ald Munro, A. E. Parkhurst, Helen S. Pittman,

A. G. Rice, A. T. Ronan, F. W. Snow, G. L.
Steele, R. R. Stratton, J. E. Talbot, E. L. Young.

COMMITTEE CONCERNED WITH PREPAYMENT MEDICAL-CARE COSTS INSURANCE — Established 1940.

J. C. McCann, *chairman*; E. S. Bagnall, P. H. Leavitt,
G. L. Schadt, J. C. Merriam (interim appoint-
ment).

COMMITTEE ON TAX-SUPPORTED MEDICAL CARE — Established 1940.

E. S. Bagnall, *chairman*; A. L. Duncombe, A. A. Hor-
nor, E. L. Hunt, W. J. Pelletier.

COMMITTEE TO MEET WITH THE MASSACHUSETTS HOSPITAL ASSOCIATION — Established 1940.

W. G. Phippen, *chairman*; Frederic Hagler, E. D.
Gardner, A. E. Parkhurst, F. W. Snow, E. A.
Adams.

COMMITTEE ON MATERNAL WELFARE — Established 1941.

J. A. Smith, *chairman*; Thomas Almy, R. L. DeNor-
mandie, Eoline C. Dubois, C. J. Duncan, M. F.
Eades, A. F. G. Edgelow, Florence L. McKay,
J. W. O'Connor, L. E. Phaneuf, G. M. Shipton,
W. R. Sisson, R. M. Smith, R. S. Titus, R. J. Wil-
liams.

COMMITTEE ON REHABILITATION — Established 1941.

W. E. Browne, *chairman*; W. M. Collins, J. J. Regan,
B. F. Andrews, R. M. Chambers, A. L. Watkins,
John Fallon.

COMMITTEE CONCERNED WITH POSTPAYMENT MEDICAL-CARE COSTS THROUGH BANKS — Established 1942.

E. S. Bagnall, *chairman*; H. G. Stetson, D. J. Ellison.

COMMITTEE TO AID THE BOSTON MEDICAL LIBRARY — Established 1942.

W. H. Robey, *chairman*; David Cheever, M. A. Tighe,
Eliot Hubbard, Jr., C. E. Mongan.

COMMITTEE TO MEET WITH THE MEDICAL ADVISORY COMMITTEE OF THE INDUSTRIAL ACCIDENT BOARD — Established 1942.

D. J. Ellison, *chairman*; G. M. Morrison, D. D. Scan-
nell.

MILITARY POSTGRADUATE COMMITTEE — Established 1942.

W. R. Ohler, *chairman*; L. E. Parkins, *secretary*; C. S.
Keefer, S. H. Proger, F. R. Ober, G. M. Morrison
(interim appointment).

COMMITTEE ON WAYS AND MEANS TO CONSERVE PHYSICIANS' ENERGIES — Established 1942.

E. S. Bagnall, *chairman*; C. F. Wilinsky, J. J. Dum-
phy.

WAR PARTICIPATION COMMITTEE — Established 1943.

W. B. Breed, *chairman*; R. R. Stratton, *vice-chairman*;
Reginald Fitz, Dwight O'Hara, M. A. Tighe, Carl
Bearse.

COMMITTEE TO AID THE DISTRICT RATIONING ADMINISTRATOR — Established 1943.

Joseph Garland, *chairman*; F. G. Brigham, F. W.
White (all interim appointments).

POSTWAR LOAN FUND COMMITTEE—Established 1943

G L Schadt, *chairman*, E P Bagg, C S Burwell,
John Homans, Eliot Hubbard, Jr, P H Leavitt,
H L Lombard, Hym in Morrison, W G Pluppen,
W F Ryan, D D Scannell, C A Sparrow, R R
Strutton, M A Tighe, C F Wilinsky

REPRESENTATIVE TO MENTAL HEALTH FOR DEFENSE OR
GANIZATION

Abraham Myerson

REPRESENTATIVE TO THE HOSPITAL COUNCIL OF BOSTON FOR
THE YEAR 1943

F H Colby

DELEGATES AND ALTERNATES TO THE HOUSE OF
DELEGATES, AMERICAN MEDICAL ASSOCIATION,
FOR 1943-1944

DELEGATES

ALTERNATES

June 1, 1942, to June 1, 1944

D D Scannell, Jamaica Plain	E S Bagnall, Groveland
Dwight O'Hara, Waltham	E L Hunt, Worcester
C E Mongan, Somerville	C J Kickham Brookline
W G Pluppen, Salem	J I B Van, Hyannis

June 1 1943 to June 1, 1945

A G Rice, Springfield	P J Sullivan, Dalton
R H Miller, Boston	John Fallon, Worcester

MASSACHUSETTS COMMITTEE OF PROCUREMENT AND
ASSIGNMENT SERVICE

(This is not a committee of the Massachusetts Medical
Society. It is here listed for purposes of information only.)

Reginald Fitz, *chairman*, H M Clute, F L Kickham
Dwight O'Hara, W H Pulsifer, B P Sweeney

MASSACHUSETTS MEDICAL SERVICE

Officers and Directors

James C McConn, MD, president
Philip M Morgan, vice president
Edmund L Tuomey, treasurer
J Harper Blaisdell, MD
Daniel J Boyle
Thomas G Brown
Thomas G Dignan
J H Humphrey
Ernest A Johnson
Harold B Leland
Charles E Mongan MD
Frank R Ober, MD
P A OConnell
Roswell F Phelps
Oliver G Pratt
Samuel A Robins, MD
R F Cahillane, executive director,
230 Congress Street, Boston

Members of the Corporation

William H Allen, MD	Roger I Lee, MD
Elmer S Bagnall, MD	Donald Munro, MD
Frederick J Barnard, MD	Dwight O'Hara, MD
Carl Bearse, MD	Ralph S Perkins, MD
William M Collins, MD	L Beverly Pond, MD
C Bertram Gay, MD	Daniel B Reardon, MD
Loring Grimes, MD	Frank W Snow, MD
Edward M Halligan, MD	George L Steele, MD
Eliot Hubbard, Jr, MD	Michael A Tighe, MD
Peirce H Leavitt, MD	

COUNCILORS FOR 1943-1944

ELECTED BY THE DISTRICT MEDICAL SOCIETIES AT THEIR
ANNUAL MEETINGS, APRIL 15 TO MAY 15, 1943

BARNSTABLE

J G Kelley, Pocasset, Barnstable County Sanatorium
V P
P M Butterfield, Harwich, A M N C
C H Keene, Chatham, Seaview St
W D Kinney, Osterville, M N C
Frank Travers, Barnstable, King's Highway, Sec

BARNSTABLE

C T Leslie, Pittsfield, 18 Bank Row, V P
J W Bunce, North Adams, 85 Main St
N N Copeland, Pittsfield, 131 North St, Sec
I S F Dodd, Pittsfield, 34 Fenn St
C F Fasce, Pittsfield, 311 North St, A M N C
C F Kernan, Pittsfield, 184 North St
J F McLaughlin, Adams, 25 Park St
Solomon Schwager, Pittsfield, 246 North St
P J Sullivan, Dalton, 471 Main St, M N C

BRISTOL NORTH

J L Murphy, Taunton, 23 Cedar St, V P, A M
N C
W H Allen, Mansfield, 70 North Main St, E C
M N C
J H Brewster, Attleboro, 178 South Main St
R M Chambers, Taunton, Taunton State Hospital
A E C
W J Morse, Jr, Attleboro 34 Sanford St Sec
W M Stobbs, Attleboro, 63 Bank St

BRISTOL SOUTH

F F Shay, Fall River, 450 Hood St, V P
G W Blood Fall River, 82 New Boston Rd
R B Butler, Fall River, 278 North Main St, A M
N C
E F Cody, New Bedford, 105 South Sixth S
M N C
J A Fournier, Fall River, 11 Choate St
E D Gardner, New Bedford, 150 Cottage St
D R Mills, Edgartown
H C Perry New Bedford, 159 Cottage St
A H Sterns, New Bedford, 31 Seventh St, Sec
I N Tilden, Mattapoisett, Barstow St
C C Tripp, New Bedford, 416 County St
P F Truesdale, Fall River, 151 Rock St
Henry Wardle, Fall River, 173 Purchase St

ESSEX NORTH

R C Hannigan, Amesbury, 41 Market St. V P
F S Bagnall Groveland 281 Main St, President
Flect

R. V. Baketel, Methuen, 7 Hampshire St.
 L. R. Chaput, Haverhill, 3 Washington Sq.
 N. F. DeCesare, Lawrence, 57 Jackson St.
 E. H. Ganley, Methuen, 251 Broadway.
 H. R. Kurth, Lawrence, 57 Jackson St., Sec.
 P. J. Look, Andover, 115 Main St.
 R. J. Neil, Methuen, 255 Broadway.
 R. C. Norris, Methuen, 247 Broadway, A. E. C.,
 A. M. N. C.
 G. L. Richardson, Haverhill, 94 Emerson St., M. N. C.
 F. W. Snow, Newburyport, 24 Essex St., E. C.
 C. F. Warren, Amesbury, 1 School St.

ESSEX SOUTH

P. E. Tivnan, Salem, 70 Washington St., V. P.
 Bernard Appel, Lynn, 281 Ocean St.
 H. A. Boyle, Middleton, Essex Sanatorium.
 D. S. Clark, Salem, 2 Oliver St., M. N. C.
 C. L. Curtis, Salem, 10 Federal St., A. E. C.
 R. E. Foss, Peabody, 125 Main St.
 Loring Grimes, Swampscott, 84 Humphrey St., E. C.
 W. R. Irving, Gloucester, 35 Middle St.
 P. P. Johnson, Beverly, 1 Monument Sq., A. M.
 N. C.
 H. M. Lowd, Swampscott, 90 Burrill St.
 B. B. Mansfield, Ipswich, 4 Green St.
 A. E. Parkhurst, Beverly, Monument Sq.
 O. S. Pettingill, Middleton, Essex Sanatorium.
 W. G. Phippen, Salem, 31 Chestnut St., Ex-Pres.
 E. D. Reynolds, Danvers, 48 High St.
 H. D. Stebbins, Salem, 26 Chestnut St., Sec.
 J. W. Trask, East Lynn, 90 Ocean St.
 C. F. Twomey, East Lynn, 80 Ocean St.
 C. A. Worthen, Lynn, 19 Park St.

FRANKLIN

A. W. Hayes, Greenfield, 78 Federal St., V. P.
 F. J. Barnard, Greenfield, 479 Main St., E. C., M. N. C.
 H. L. Craft, Ashfield, Sec.
 H. M. Kemp, Greenfield, 42 Franklin St.
 W. J. Pelletier, Turners Falls, 113 Ave. A, A. E. C.,
 A. M. N. C.
 H. G. Stetson, Greenfield, 39 Federal St., Ex-Pres.

HAMPDEN

E. A. Knowlton, Holyoke, 207 Elm St., V. P., A. E. C.
 F. H. Allen, Holyoke, 16 Fairfield St.
 E. P. Bagg, Holyoke, 207 Elm St., A. M. N. C.
 W. C. Barnes, Springfield, 146 Chestnut St., Sec.
 J. M. Birnie, Springfield, 146 Chestnut St., Ex-Pres.
 H. F. Byrnes, Springfield, 6 Chestnut St.
 W. A. R. Chapin, Springfield, 121 Chestnut St.
 J. L. Chereskin, Springfield, 333 Bridge St.
 G. B. Corcoran, West Springfield, 84 Park St.
 A. J. Douglas, Westfield, 93 Elm St.
 E. C. Dubois, Springfield, 174 Buckingham St.
 Adolph Franz, Jr., Holyoke, 276 Maple St.
 G. L. Gabler, Holyoke, 4 Bullard Ave.
 P. E. Gear, Holyoke, 188 Chestnut St.
 Frederic Hagler, Springfield, 20 Maple St.
 G. D. Henderson, Holyoke, 312 Maple St.
 F. S. Hopkins, Springfield, 146 Chestnut St.
 Charles Jurist, Springfield, 70 Chestnut St.
 M. W. Pearson, Ware, 19 Pleasant St.
 A. G. Rice, Springfield, 146 Chestnut St., M. N. C.
 G. L. Schadt, Springfield, 44 Chestnut St., Ex-Pres.
 G. L. Steele, Springfield, 20 Maple St., E. C.

HAMPSHIRE

A. N. Ball, Northampton, State Hospital, V. P.
 A. J. Bonneville, Hatfield, 60 Main St.
 J. D. Collins, Northampton, 187 Main St., A. E. C.,
 A. M. N. C.
 W. M. Dobson, Northampton, Veterans Administration
 Facility.
 L. B. Pond, Easthampton, 115 Main St., E. C.,
 M. N. C.
 Mary P. Snook, Chesterfield, Sec.

MIDDLESEX EAST

R. M. Burgoyne, Winchester, 15 Washington St., V. P.
 J. H. Blaisdell, Winchester, Office Boston, 45 Bay
 State Rd.
 C. W. De Wolf, Melrose, 8 Porter St.
 Richard Dutton, Wakefield, 33 Avon St., A. E. C.
 E. M. Halligan, Reading, 37 Salem St., E. C., A. M.
 N. C.
 R. W. Layton, Melrose, 8 Porter St., Sec.
 M. J. Quinn, Winchester, 44 Church St.
 R. R. Stratton, Melrose, 538 Lynn Fells Parkway,
 M. N. C., C.
 J. M. Wilcox, Woburn, 6 Bennett St.

MIDDLESEX NORTH

H. M. Larrabee, Lowell, 9 Central St., V. P.
 H. R. Coburn, Lowell, 202 Merrimack St.
 W. M. Collins, Lowell, 174 Central St., E. C.
 D. J. Ellison, Lowell, 8 Merrimack St.
 A. R. Gardner, Lowell, 16 Shattuck St.
 B. D. Leahey, Lowell, 9 Central St., Sec.
 W. F. Ryan, Lowell, 219 Central St.
 W. H. Sherman, Lowell, 9 Central St., A. M. N. C.
 M. A. Tighe, Lowell, 9 Central St., Secretary,
 M. N. C.

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H. G. Giddings, Newton Centre, Office Boston, 270
 Commonwealth Ave., V. P.
 C. F. Atwood, Arlington, 821 Massachusetts Ave.
 E. W. Barron, Malden, Office Boston, 20 Ash St.
 W. B. Bartlett, Concord, 28 Monument St.
 Harris Bass, Everett, 351 Broadway.
 J. M. Baty, Belmont, Office Brookline, 1101 Beacon
 St.
 J. D. Bennett, West Somerville, 72 College Ave.
 S. M. Biddle, Cambridge, 206 Huron Ave.
 E. H. Bigelow, Framingham, Hotel Kendall, Ex-Pres.
 W. O. Blanchard, Newton, 465 Centre St.
 G. F. H. Bowers, Newton Highlands, 156 Woodward
 St.
 Madelaine R. Brown, Cambridge, Office Boston, 264
 Beacon St.
 R. W. Buck, Waban, Office Boston, 5 Bay State Rd.
 E. J. Butler, Cambridge, 25 Garden St.
 J. F. Casey, Allston, Office Boston, 475 Common-
 wealth Ave.
 J. J. Cochran, Natick, 15 West Central St.
 B. F. Conley, Malden, 51 Main St.
 H. F. Day, Cambridge, 34 Kirkland St.
 C. L. Derick, Newton Highlands, Office Boston, 412
 Beacon St.
 Emilio D'Errico, Medford, Office Boston, 27 Bay
 State Rd.
 J. G. Downing, Newton, Office Boston, 520 Common-
 wealth Ave.

C W. Finnerty, West Somerville, 5 Pearson Rd
 H Q Gallupe, Waltham, 751 Main St
 Stanton Garfield, Concord, 20 Sudbury St
 F W Gay, Malden, 20 Park St
 H W Godfrey, Auburndale, 14 Hancock St
 J L Golden, Medford, 86 Forest St
 A D Guthrie, Medford, 408 Salem St
 Eliot Hubbard, Jr, Cambridge, 29 Highland St
 Treasurer
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 A A Levi, Newton, Office Boston, 481 Beacon St
 Sec
 F P Lowry, Newton, 313 Washington St
 A N Makechmie, Cambridge, 14 Upland Rd
 J C Merriam, Framingham, 198 Union Ave, A M
 N C
 Dudley Merrill, Cambridge, 51 Brattle St.
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 wealth Ave, C
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 Hospital
 E J O'Brien, Jr, Newton, Office Boston, 270 Com
 monwealth Ave.
 Dwight O'Hara, Waltham, Office Boston, 416 Hunt
 ington Ave, E C, M N C, C
 Fabyan Packard, Belmont, Office Boston, Soldiers'
 Field
 L G Paul, Newton Centre, Office Boston, 270 Com
 monwealth Ave.
 T C Reilly, Marlboro, 6 Newton St
 S H Remick, Waltham, 735 Trapelo Rd, A E C
 Max Ritvo, Newton, Office Boston, 485 Common
 wealth Ave
 E H Robbins, Somerville, 334 Broadway
 E S A Robinson, Newton Centre, Office Jamaica
 Plain, 375 South St.
 M J Schlesinger, Newton, Office Boston, 330 Brook
 line Ave.
 E. W Small, Belmont, 68 Leonard St.
 H W Thayer, Newtonville, 355 Walnut St
 A B Toppan, Watertown, 289 Mt Auburn St
 J E Vance, Natick, Office Boston, 510 Common
 wealth Ave
 Fresenius Van Nuys, Weston, 338 Boston Post Rd
 C F Walcott, Cambridge, 81 Sparks St
 B M Wein, Newton, Office Boston, 471 Common
 wealth Ave.
 B S Wood, Weston, Office Waltham, 751 Main St.
 Alfred Worcester, Waltham, 314 Bacon St, Ex Pres
 Hovhannes Zovickian, Watertown, 528 Mt Auburn
 St

NORFOLK

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 Commonwealth Ave., V P
 J R Barry, West Roxbury, 1857 Centre St
 Carl Bearse, Boston, 483 Beacon St, E C
 Arthur Berk, Brookline, Office Boston, 270 Com
 monwealth Ave.
 M I Berman, Dorchester, 1071A Blue Hill Ave
 G F Blood, Roslindale, 20 Belgrade Ave
 D J Collins, Norwood, 100 Day St.

L F Curran, Dorchester, Office Boston, 409 Marl
 boro St.
 William Dameshek, Brookline, Office Boston, 371
 Commonwealth Ave
 F P Denny, Brookline, 111 High St, C
 G L Doherty, West Roxbury, Office Boston, 466
 Commonwealth Ave
 Albert Ehrenfried, Brookline, Office Boston, 520 Bea
 con St
 H M Emmons, Needham, Office Boston, 354 Com
 monwealth Ave.
 Morris Frank, Roxbury, 173 Humboldt Ave
 Susannah Friedman, Roxbury, Office Boston, 485
 Commonwealth Ave.
 B A Godvin, Jamaica Plain, Office Boston, 483 Bea
 con St
 D C Goldfarb, Brookline, Office Boston, 483 Bea
 con St
 J B Hall, Roxbury, 60 Windsor St.
 H B Harris, East Milton, Office Dorchester, 487
 Columbia Rd
 R J Heffernan, Jamaica Plain, Office Brookline, 1101
 Beacon St.
 H J Inghs, Chestnut Hill, Office Boston, 43 Bay
 State Rd, A M N C
 P J Jakmaub, Milton, Office South Boston, 509
 Broadway
 I R Jankelson, Jamaica Plain, Office Boston, 483
 Beacon St
 C J Kickham, Brookline, Office Boston, 524 Com
 monwealth Ave
 C J E Kickham, Jamaica Plain, Office Boston, 12
 Bay State Rd
 E L Kickham, Brookline, Office Boston, 270 Com
 monwealth Ave
 D S Luce, Canton, 553 Washington St
 C M Lydon, Dorchester, 276 Bowdoin St
 D L Lynch, Roslindale, Office Boston, 245 State St
 T F P Lyons, Milton, Office Boston, 270 Com
 monwealth Ave, Sec
 F P McCarthy, Milton, Office Boston, 371 Common
 wealth Ave
 H L McCarthy, West Roxbury, Office Boston, 479
 Beacon St.
 R T Monroe, Brookline, Office Boston, 270 Com
 monwealth Ave, C
 F J Moran, Dedham, 395 Washington St
 Hyman Morrison, Roxbury, Office Boston, 483 Bea
 con St
 D J Mullane, Jamaica Plain, 776 Centre St.
 M W O'Connell, West Roxbury, Office Boston, Bos
 ton City Hospital
 G W Papen, Brookline, Office Boston, 31 Milk St.
 H C Petterson, West Roxbury, Office Boston, 29 Bay
 State Rd
 Frederick Reis, Jamaica Plain, Office Boston, 416
 Huntington Ave.
 S A Robins, Roxbury, Office Boston, 636 Beacon St.
 D D Scannell, Jamaica Plain, Office Boston, 475
 Commonwealth Ave, M N C
 J A Seth, Milton, Office Boston, 47 Bay State Rd
 Kathleeyne S Snow, Jamaica Plain, Office Boston, 466
 Commonwealth Ave
 J W Spellman, Chestnut Hill, Office Brookline,
 1101 Beacon St.
 M H Spellman, Jamaica Plain, Office Boston, 475
 Commonwealth Ave

- J. P. Treanor, Jr., Jamaica Plain, Office Brookline, 1101 Beacon St.
 W. J. Walton, Dorchester, 106 Bowdoin St.
 S. H. Weiner, Roxbury, Office Boston, 524 Commonwealth Ave.
 N. A. Welch, West Roxbury, Office Boston, 520 Commonwealth Ave., Assistant Treasurer.

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 C. S. Adams, Wollaston, 62 Brooks St.
 F. A. Bartlett, Wollaston, 308 Beale St.
 D. L. Belding, Hingham, Office Boston, 80 East Concord St.
 R. L. Cook, Quincy, 38 Russell Park.
 F. W. Crawford, Holbrook, 98 North Franklin St.
 E. K. Jenkins, South Braintree, Norfolk County Hospital, Sec.
 J. E. Knowlton, Quincy, 579 Hancock St.
 L. W. Pease, Weymouth, 135 Webb St.
 D. B. Reardon, Quincy, 1186 Hancock St., Vice-President, E. C., M. N. C.
 H. A. Robinson, Hingham, 205 North St., A. E. C., A. M. N. C.

PLYMOUTH

- E. L. Perry, Middleboro, 39 Oak St., V. P.
 J. E. Brady, Brockton, 231 Main St.
 G. A. Buckley, Brockton, 12 Cottage St.
 P. B. Kelly, Plymouth, 27 Court St.
 P. H. Leavitt, Brockton, 129 West Elm St., E. C., A. M. N. C.
 C. D. McCann, Brockton, 12 Cottage St., A. E. C.
 R. C. McLeod, Brockton, Goddard Hospital, Sec.
 J. J. McNamara, Brockton, 231 Main St.
 G. A. Moore, Brockton, 167 Newbury St.
 W. H. Pulsifer, Whitman, 26 Park Ave., M. N. C.

SUFFOLK

- J. P. O'Hare, Boston, 520 Commonwealth Ave., V. P.
 A. W. Allen, Boston, 264 Beacon St., C.
 J. W. Bartol, Boston, 1 Chestnut St., Ex-Pres.
 W. B. Breed, Boston, 264 Beacon St., M. N. C.
 W. J. Brickley, Boston, 524 Commonwealth Ave.
 W. E. Browne, Boston, 587 Beacon St.
 G. C. Caner, Boston, 63 Marlboro St.
 E. M. Chapman, Boston, 270 Commonwealth Ave.
 David Cheever, Boston, 193 Marlboro St.
 H. M. Clute, Boston, 171 Bay State Rd.
 Pasquale Costanza, East Boston, 238 Maverick St.
 N. W. Faxon, Boston, Massachusetts General Hospital.
 G. B. Fenwick, Chelsea, 38 Cary Ave.
 Jacob Fine, Boston, 330 Brookline Ave.
 Reginald Fitz, Boston, 319 Longwood Ave.
 Maurice Fremont-Smith, Boston, 12 Hereford St.
 Channing Frothingham, Boston, Office Jamaica Plain, 1153 Centre St., Ex-Pres.
 Joseph Garland, Boston, 266 Beacon St.
 R. L. Goodale, Boston, 330 Dartmouth St., Sec.
 F. C. Hall, Boston, 372 Marlboro St., C.
 A. A. Hornor, Boston, 319 Longwood Ave., A. M. N. C.
 L. M. Hurxthal, Boston, 605 Commonwealth Ave.
 C. S. Keefer, Boston, 65 East Newton St.
 H. A. Kelly, Winthrop, 200 Pleasant St.

- R. I. Lee, Boston, 264 Beacon St., President.
 C. C. Lund, Boston, 319 Longwood Ave., A. E. C.
 W. J. Mixter, Boston, 319 Longwood Ave.
 Donald Munro, Boston, 818 Harrison Ave., E. C.
 H. L. Musgrave, Revere, 622 Beach St.
 H. F. Newton, Boston, 319 Longwood Ave., C.
 R. N. Nye, Boston, 8 Fenway.
 F. R. Ober, Boston, 234 Marlboro St., Ex-Pres.
 F. W. O'Brien, Boston, 465 Beacon St.
 L. E. Parkins, Boston, 12 Bay State Rd.
 L. E. Phaneuf, Boston, 270 Commonwealth Ave.
 Helen S. Pittman, Boston, 412 Beacon St.
 W. H. Robey, Boston, 202 Commonwealth Ave., Ex-Pres., C.
 H. F. Root, Boston, 81 Bay State Rd.
 R. M. Smith, Boston, 330 Dartmouth St., C.
 M. C. Sosman, Boston, 721 Huntington Ave.
 E. F. Timmins, South Boston, 527 Broadway.
 J. J. Todd, Boston, 479 Beacon St.
 S. N. Vose, Boston, 29 Bay State Rd.
 Conrad Wesselhoeft, Boston, 315 Marlboro St.
 C. F. Wilinsky, Boston, 330 Brookline Ave.

WORCESTER

- A. E. O'Connell, Worcester, 390 Main St., V. P.
 C. R. Abbott, Clinton, 60 Walnut St.
 B. H. Alton, Worcester, 27 Elm St.
 B. F. Andrews, Worcester, 36 Pleasant St.
 J. I. Ashkins, Milford, 36 Pine St.
 A. W. Atwood, Worcester, 390 Main St.
 George Ballantyne, Worcester, 27 Elm St.
 Gordon Berry, Worcester, 36 Pleasant St., A. E. C.
 W. P. Bowers, Clinton, 264 Chestnut St., Ex-Pres.
 L. R. Bragg, Webster, 260 Main St.
 P. H. Cook, Worcester, 27 Elm St.
 G. A. Dix, Worcester, 6 Ashland St.
 J. J. Dumphy, Worcester, 390 Main St.
 J. M. Fallon, Worcester, 390 Main St.
 L. M. Felton, Worcester, 36 Pleasant St.
 E. R. Leib, Worcester, 36 Pleasant St.
 L. P. Leland, Worcester, 36 Pleasant St., Sec.
 W. F. Lynch, Worcester, 390 Main St., A. M. N. C.
 J. C. McCann, Worcester, 390 Main St.
 H. L. Paine, North Grafton, Grafton State Hospital.
 R. S. Perkins, Worcester, 10 Hackfeld Rd., E. C.
 C. A. Sparrow, Worcester, 21 West St.
 O. H. Stansfield, Worcester, 36 Pleasant St.
 R. J. Ward, Worcester, 9 Bellevue St.
 R. P. Watkins, Worcester, 332 Main St., M. N. C.
 S. B. Woodward, Worcester, 58 Pearl St., Ex-Pres.

WORCESTER NORTH

- H. D. Bone, Gardner, 19 Pleasant St., V. P.
 E. A. Adams, Fitchburg, 44 Oliver St., Sec.
 C. B. Gay, Fitchburg, 62 Day St., E. C.
 G. P. Keaveny, Fitchburg, 62 Fox St., A. M. N. C.
 F. A. Reynolds, Athol, 43 Cottage St., A. E. C.
 J. G. Simmons, Fitchburg, 30 Myrtle Ave.
 B. P. Swecney, Leominster, 5 Gardner Place, M. N. C.

The initials E. C. following the name of a councilor indicate that he is a member of the Executive Committee, and A. E. C. that he is an alternate member of the Executive Committee; M. N. C. that he is a member of the Committee on Nominations and A. M. N. C. that he is an alternate member of the Committee on Nominations; V. P. that a member is a councilor by virtue of his office as president of a district society and so vice-president of the general society; C. by virtue of his office as chairman of a standing committee; Sec. by virtue of his office as secretary of a district society and Ex-Pres. by virtue of being a past president.

CENSORS FOR 1943-1944

BARNSTABLE

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 F F Curry, Sagamore
 C E Harris, Hyannis
 J I B Vail, Hyannis
 D H Hiebert, Provincetown

BERKSHIRE

I S F Dodd, Pittsfield, *supervisor*
 M M Brown, North Adams
 W T Frawley, Pittsfield
 M S Lisner, Pittsfield
 M T Cavanaugh, Great Barrington

BRISTOL NORTH

W H Allen, Mansfield, *supervisor*
 L E Butler, Taunton
 A J Leddy, Taunton
 H L Rich, Attleboro
 W M Stobbs, Attleboro

BRISTOL SOUTH

Henry Wardle, Fall River, *supervisor*
 E A McCarthy, Fall River
 C C Persons, New Bedford
 W F MacKnight, Fall River
 F M Howes, New Bedford

ESSEX NORTH

R V Baketel, Methuen, *supervisor*
 L C Pearce, Newburyport
 F A O'Reilly, Lawrence
 E M Gale, Merrimac
 W W Ferrin, Haverhill

ESSEX SOUTH

A E Parkhurst, Beverly, *supervisor*
 J G Adams, Salem
 C A Worthen, Lynn
 W C Inman, Danvers
 I B Hull, Gloucester

FRANKLIN

W J Pelleuer, Turners Falls, *supervisor*
 A H Wright, Northfield
 J E Moran, Greenfield
 A H Ellis, Greenfield
 P N Freeman, Greenfield

HAMPTON

Frederic Hagler, Springfield, *supervisor*
 G F Dalton, Springfield
 W J Dillon, Springfield
 P M Moriarty, Chicopee
 G D Henderson, Holyoke

HAMPSHIRE

A J Bonneville, Hatfield, *supervisor*
 M E Cooney, Northampton
 J E Hayes, Northampton
 T F Corriden, Northampton
 C H Wheeler, Hydenville

MIDDLESEX EAST

M J Quinn, Winchester, *supervisor*
 J L Anderson, Reading
 C E Montague, Wakefield
 J H Fay, Melrose
 S H Moses, Winchester

MIDDLESEX NORTH

W F Ryan, Lowell, *supervisor*
 F R Brady, Lowell
 R C Stewart, Lowell
 H L Leland, Lowell
 A G Scoboria, Lowell

MIDDLESEX SOUTH

H Q Gallupe, Waltham, *supervisor*
 C W Finnerty, West Somerville
 A N Makechne, Cambridge
 J E Vance, Natick
 H W Thayer, Newtonville

NORFOLK

Hyman Morrison, Roxbury, *supervisor*
 C J Kickham, Brookline
 C L Allard, Dorchester
 Saul Berman, Chestnut Hill
 Kathlyne S Snow, Jamaica Plain

NORFOLK SOUTH

C S Adams, Wollaston, *supervisor*
 D L Belding, Hingham
 C J Lynch, Quincy
 D J Bailey, Weymouth
 W L Sargent, Quincy

PLYMOUTH

G A Buckley, Brockton, *supervisor*
 J H Dunn, Rockland
 B H Peirce, South Hanson
 A W Carr, Bridgewater
 J A Pettey, Brockton

SUFFOLK

Donald Munro, Boston, *supervisor*
 A J A Campbell, Boston
 J H Pratt, Boston
 A W Reggio, Boston
 W E Browne, Boston

WORCESTER

G A Div, Worcester, *supervisor*
 D G Ljungberg, Worcester
 J T Brosnan, Worcester
 B H Flower, Shrewsbury
 R S Newton, Westboro

WORCESTER NORTH

C B Gav, Fitchburg, *supervisor*
 F J Djerf, Fitchburg
 G P Keaveny, Fitchburg
 F A Reynolds, Athol
 J A McLean, Ayer

VICE-PRESIDENTS OF THE MASSACHUSETTS
MEDICAL SOCIETY (*Ex-Officiis*)
FOR 1943-1944

PRESIDENTS OF DISTRICT MEDICAL SOCIETIES
(Arranged according to seniority of fellowship
in the Massachusetts Medical Society)

MIDDLESEX NORTH — H. M. Larrabee, Lowell.
WORCESTER — A. E. O'Connell, Worcester.
BERKSHIRE — C. T. Leslie, Pittsfield.
MIDDLESEX SOUTH — H. G. Giddings, Newton Centre.
HAMPDEN — E. A. Knowlton, Holyoke.
HAMPSHIRE — A. N. Ball, Northampton.
BRISTOL NORTH — J. L. Murphy, Taunton.
SUFFOLK — J. P. O'Hare, Boston.
NORFOLK SOUTH — G. V. Higgins, Randolph.
WORCESTER NORTH — H. D. Bone, Gardner.
NORFOLK — J. C. V. Fisher, West Roxbury.
BRISTOL SOUTH — E. F. Shay, Fall River.
MIDDLESEX EAST — R. M. Burgoyne, Winchester.
FRANKLIN — A. W. Hayes, Greenfield.
ESSEX NORTH — R. C. Hannigen, Amesbury.
PLYMOUTH — E. L. Perry, Middleboro.
BARNSTABLE — J. G. Kelley, Pocasset.
ESSEX SOUTH — P. E. Tivnan, Salem.

COMMISSIONERS OF TRIAL FOR 1943-1944

BARNSTABLE — F. O. Cass, Provincetown.
BERKSHIRE — J. B. Thomes, Pittsfield.
BRISTOL NORTH — J. W. Cook, Mansfield.
BRISTOL SOUTH — A. C. Lewis, Fall River.
ESSEX NORTH — F. W. Anthony, Haverhill.
ESSEX SOUTH — O. C. Blair, Lynn.
FRANKLIN — K. W. D. Jacobus, Turners Falls.
HAMPDEN — J. M. Birnie, Springfield.
HAMPSHIRE — E. H. Copeland, Northampton.
MIDDLESEX EAST — W. H. Keleher, Woburn.
MIDDLESEX NORTH — J. F. Boyle, Lowell.
MIDDLESEX SOUTH — H. P. Stevens, Cambridge.
NORFOLK — W. J. Walton, Dorchester.
NORFOLK SOUTH — F. A. Bartlett, Wollaston.
PLYMOUTH — J. A. Carriuolo, Brockton.
SUFFOLK — J. R. Torbert, Boston.
WORCESTER — W. P. Bowers, Clinton.
WORCESTER NORTH — A. P. Lachance, Gardner.

OFFICERS OF THE SECTIONS FOR 1944

ELECTED BY THE SECTIONS

(The street addresses may be obtained from the
Directory of Officers and Fellows)

SECTION OF MEDICINE

Chairman, George D. Henderson, Holyoke; *secretary*,
Albert A. Hornor, Boston.

SECTION OF SURGERY

Chairman, Howard M. Clute, Boston; *secretary*,
Charles F. Twomey, East Lynn.

Executive Committee — Archibald M. Fraser, Boston
(1 year); Stanley J. G. Nowak, Belmont and Bos-
ton (2 years); Edward L. Young, Jr., Brookline
and Boston (3 years).

SECTION OF PEDIATRICS

Chairman, Leroy T. Stokes, Haverhill; *secretary*, Ger-
ald N. Hoeffel, Cambridge.

Executive Committee — Harold L. Higgins, Newton,
chairman; Philip H. Sylvester, Boston, James Mar-
vin Baty, Belmont and Brookline.

SECTION OF OBSTETRICS AND GYNECOLOGY

Chairman, Christopher J. Duncan, Brookline; *vice-
chairman*, Arthur F. G. Edgelow, Springfield;
secretary, George Van S. Smith, Brookline.

SECTION OF RADIOLOGY

Chairman, Stanley A. Wilson, Salem; *secretary*,
George Levene, Chestnut Hill and Boston.

SECTION OF PHYSIOTHERAPY

Chairman, Wilmot L. Marden, Lynn; *secretary*, How-
ard Moore, Newton and Boston.

SECTION OF DERMATOLOGY AND SYPHILOLOGY

Chairman, John G. Downing, Newton and Boston;
secretary, G. Marshall Crawford, Lincoln and
Brookline.

OFFICERS OF THE DISTRICT MEDICAL SOCIETIES
FOR 1943-1944

ELECTED BY THE DISTRICT MEDICAL SOCIETIES AT THEIR
ANNUAL MEETINGS IN 1943

(The street addresses may be obtained from the
Directory of Officers and Fellows)

BARNSTABLE — *President*, Julius G. Kelley, Pocasset;
vice-president, Joseph N. Kelly, Orleans; *secretary*, Frank
Travers, Barnstable; *treasurer*, Harold F. Rowley, Har-
wich Port; *librarian*, Carroll H. Keene, Chatham.

BERKSHIRE — *President*, Charles T. Leslie, Pittsfield;
vice-president, Floyd R. Smith, Pittsfield; *secretary*,
N. Newall Copeland, Pittsfield; *treasurer*, Daniel N. Beers,
Pittsfield; *legislative and public-relations councilor*, Pat-
rick J. Sullivan, Dalton.

BRISTOL NORTH — *President*, Joseph L. Murphy, Taun-
ton; *vice-president*, William M. Stobbs, Attleboro; *sec-
retary*, William J. Morse, Jr., Attleboro; *treasurer*, Joseph
V. Chatigny, Taunton; *executive councilor*, William H.
Allen, Mansfield; *legislative councilor*, Joseph L. Murphy,
Taunton; *public-relations councilor*, James H. Brewster,
Attleboro.

BRISTOL SOUTH — *President*, Edward F. Shay, Fall
River; *vice-president*, Russell Wood, New Bedford; *sec-
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public-relations councilor, Harold E. Perry, New Bedford

ESSEX NORTH — *President*, Robert C. Hannigen, Ames-
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Harold R. Kurth, Lawrence; *treasurer*, Guy L. Richard-

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Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 29291

PRESENTATION OF CASE

A fifty-three-year-old housewife entered the hospital because of fluid in the right chest.

Approximately three months prior to admission, following a cat scratch on the right thigh, she developed a tender red swelling of the thigh that spread in the next three days to the knee and upper calf. Simultaneously an "erysipeloid" reaction developed on the medial aspect of the left upper thigh. Her physician treated her with sulfadiazine by mouth for a week and the inflammation subsided. However, several days later the entire right leg became warm, swollen and mottled, and two or three days later the left leg assumed a similar appearance. After five weeks of bed rest most of the infection subsided. Three and a half weeks prior to admission, the patient became progressively short of breath, and ten days later at a community hospital 900 cc. of bloody fluid were withdrawn from the right pleural cavity. She felt better after the tap and returned home. Three days prior to admission marked breathlessness returned, and since the pleural fluid had reaccumulated, she was referred to this hospital for further care. During the illness her temperature usually ranged from 99.4 to 100°F., but on two occasions at night it rose to 103. There was no hemoptysis, chills, weight loss or night sweats.

The family and past histories were noncontributory.

Physical examination revealed a somewhat obese, slightly dyspneic woman who coughed occasionally but did not raise any sputum. The chest was large, and the anteroposterior diameter increased. There was limitation of expansion of the chest, particularly on the right. Flatness was percussed over the right chest posteriorly as high as the scapula. In this area the breath and voice sounds were inaudible. Anteriorly over the right apex and posteriorly over the left lower chest and just above the area of flatness on the right there were showers of fine crackling rales, principally on expiration, that did not clear after coughing.

*On leave of absence.

A blowing systolic murmur was heard over the entire precordium but best in the tricuspid area. There was moderate tenderness to deep palpation in both lower quadrants of the abdomen, and there was a sense of resistance in the lower mid-abdomen; no definite masses were felt. The right liver edge was percussed four fingerbreadths below the costal margin. Over both knees, the lateral aspect of the right ankle and the left calf there was a macular, bright-red, smooth rash. There was no edema. Homans's sign for thrombophlebitis was negative.

The blood pressure was 175 systolic, 95 diastolic. The temperature was 101.6°F., the pulse 112, and the respirations 31.

The red-cell count was 4,950,000, and a stained smear showed 64 per cent neutrophils. The urine was normal. A blood Hinton test was negative. The protein was 4.2 gm., the sugar 108 mg., and the nonprotein nitrogen 33 mg. per 100 cc.

An electrocardiogram showed normal sinus rhythm, with a rate of 115. The PR interval was 0.16 second. The T wave was low in Leads 1, 2, and 3, and inverted in Lead 4; there was slight right-axis deviation.

An x-ray film of the chest showed a moderate amount of fluid and air in the right pleural cavity that collapsed the right lung to about half its usual size. The fluid rose to the level of the third rib anteriorly. The right half of the diaphragm was elevated and showed considerable limitation in motion. There was some increase in the markings of the left lung field; otherwise this lung was not remarkable. The heart and mediastinum were slightly displaced to the left. The carina was not widened. The right main bronchus was not sufficiently well visualized to determine intrinsic disease. X-ray films and laminograms after removal of 1200 cc. of bloody xanthochromic fluid from the right chest revealed an apparent mass at the right hilus that extended into the right upper lobe.

During hospitalization the patient seemed quite short of breath but had few complaints. The temperature was usually 100°F.; the pulse ranged from 80 to 125, and the respirations from 20 to 45.

On the twelfth hospital day the patient suddenly began to sweat profusely and the pulse became rapid and thready. She denied pain. The cardiac apical rate was 120, and there was a prominent gallop rhythm. Respirations were 35, and the systolic blood pressure was 80. The extremities were cold and clammy. She was treated supportively and seemed somewhat better. Half an hour later the left arm became blue, painful and cold, and no brachial or radial pulse could be felt. She failed rapidly, became cyanotic and dyspneic, and died five minutes later.

DIFFERENTIAL DIAGNOSIS

DR CHESTER M. JONES: To me this history outlines a very curious sequence of events. It is obvious that the patient had some sort of infection in the lower extremities. She subsequently developed a bloody pleural effusion. At no time did she have pain in the chest, which is one of the striking things in the story. Three months after the onset of her first symptoms, she was admitted to the hospital, still with fluid in the chest, but at that time there was no swelling of the legs, although it had been present about two months previously. There still was, however, evidence of an inflammatory process described as an erythematous rash. The chest fluid was first bloody and later bloody and xanthochromic, indicating that blood had been there for a long time and that some of the hemoglobin had changed to bile pigment. I assume that the pneumothorax developed when air was introduced during the chest tap. Such a finding complicates the picture somewhat. Then with the terminal event, which came on suddenly, again there was no pain. If one states these facts in sequence—infection of the right thigh, something that was called erysipelas, subsequently warmth, swelling and mottling of the lower legs, first on the right and then on the left, and finally something in the chest—it is reasonable to say that this woman had infection, then thrombophlebitis in the deep veins of the legs, probably the superficial femoral vein, and finally pulmonary embolism.

There are several queer things, however, about this diagnosis. She never had any pain, either in the legs or in the chest. Furthermore, two months after the first swelling and redness appeared in the legs, we are told that she had no further swelling and the Homans's sign for phlebitis was negative. That does not prove there was not a deep phlebitis. Certainly we have seen numerous cases in which there was thrombophlebitis productive of a pulmonary embolus and in which we were unable to recognize the thrombophlebitis on the basis of physical signs in the leg. It is still more curious that when examined here there was no demonstrable edema, although more than once I have seen pulmonary embolism due to phlebitis of the deep veins of the leg that was not accompanied by demonstrable edema. It is not the thing to expect, however.

I should like to see the x-ray films of the chest at this time and raise the question whether the apparent mass described is suggestive of a primary bronchiogenic carcinoma. If so, we may be dealing with several diagnoses here instead of one. The collapse of the lung, apparently due to air and fluid in the pleural cavity, explains why the

diaphragm was high. After removal of a lot of fluid the lung was still collapsed, apparently because the diaphragm was very high.

DR LAURENCE L. ROBBINS: The diaphragm is high, but I doubt that it has anything to do with the air that is in the pleural cavity. Usually with collapse of the lung due to fluid and air in the pleural cavity the lung is compressed mechanically, and under these circumstances one would expect the right half of the diaphragm to be low.

DR JONES: Yes; but if there is compression against the collapse of the lung and compression of a bronchus that might cause a high diaphragm rather than a low one.

DR ROBBINS: Usually that happens when there is no fluid or air.

DR JONES: Do you think it is correct to say that the diaphragm is high?

DR ROBBINS: Yes.

DR JONES: The laminograms show something definite?

DR ROBBINS: Yes. Although they are not satisfactory in the usual sense, because we cannot see the outline of the right main bronchus or the trachea, they show a definite line in the area that should represent the base of the right upper lobe, with partial consolidation or something invading it. The shadow in the region of the hilus suggests enlarged lymph nodes. In this film it has a lobulated margin.

DR JONES: If there were a bronchiogenic carcinoma producing collapse of a portion of the lung, and a mass at the hilus, would you not expect a slightly different picture?

DR ROBBINS: Not necessarily. If this is a bronchiogenic carcinoma, I should say that it was located fairly close to the right upper lobe division, that is, in one of the secondary bronchi of the right upper lobe, and that the hilar mass was probably metastatic or direct extension of the tumor.

DR JONES: The thing that amazes me is the relatively painless and insidious occurrence of the bloody fluid in the pleural cavity. The absence of hemoptysis, pain and sudden onset in the early part of the story is I believe rather striking clinical evidence against pulmonary embolism. Furthermore, bloody fluid is quite unusual in the presence of pulmonary infarction unless the infarct is very large, or close to the pleural surface, in which case it is surprising there was no pain. I believe that a bloody pleural effusion can follow a peripheral infarction, but this sequence of events is rather unusual with the sort of story that this patient presented.

DR BENJAMIN CASTLEMAN: All bland infarcts extend to the pleural surface of the lung, and

only about 15 per cent of them are directly associated with pleural fluid, which may or may not be hemorrhagic.

DR. JONES: On the basis of the x-ray findings, it seems to me that this is not the picture one would expect with a pulmonary infarction or multiple pulmonary emboli. From the story I am more inclined to link the hilar lesion, which is definite in the x-ray film, with a malignant process, and I believe that bronchiogenic carcinoma is the most logical diagnosis. If that is so, it explains the bloody pleural fluid. I think it is fair to say that in addition to everything else, this patient had hypertensive heart disease and presumably was asthmatic. I think the cause of death may well have been an acute pulmonary embolus or coronary thrombosis. However, the rapidity with which the symptoms ensued makes me think that the terminal episode was associated with pulmonary embolism.

The electrocardiogram is going to be difficult to interpret. There was definite displacement of the heart when the electrocardiogram was taken. It had moved appreciably to the left, but the striking thing is, even with displacement of the heart to the left, that the electrocardiogram is recorded as showing right-axis deviation, when one would expect left-axis deviation. But in spite of the right-axis deviation, there was a low T wave in the first three leads and inversion of the T wave in Lead 4. That I believe is entirely consistent with right-sided heart failure and not at all inconsistent with pulmonary embolism. There was heart failure, as evidenced by the large liver, and it was undoubtedly right sided—let us say a cor pulmonale as a result of something going on in the chest. One of the conditions in which right-sided heart failure develops rather acutely is in association with pulmonary emboli.

I cannot make a diagnosis with any degree of assurance, but I believe that the patient had a thrombophlebitis of the lower extremities and I should not be at all surprised if there were pulmonary emboli. I also believe there was a terminal pulmonary embolism, together with right-sided heart failure. The systolic murmur over the tricuspid area is interesting; I think it was due to an incompetent or insufficient tricuspid valve and not necessarily to endocarditis. The mass in the mediastinum is probably better explained on the basis of malignancy than of anything else.

DR. JACOB LERMAN: How do you explain the final episode of arterial embolus to the left arm unless you assume endocarditis?

DR. JONES: That was a curious thing. It was noted distinctly as a terminal event, and I do not know how to interpret it. Half an hour after the

sudden collapse, the left arm was noted to be cold, blue and so forth. Of course one can say there was an embolic occlusion of the brachial artery associated with acute circulatory collapse. The systolic blood pressure dropped from 175 to 80.

A PHYSICIAN: How about something in the pulmonary veins? I know such lesions are rare.

DR. CASTLEMAN: Thrombi in the smaller pulmonary veins occur probably a lot more frequently than we realize.

A PHYSICIAN: I was thinking of embolus from the main pulmonary veins.

DR. CASTLEMAN: I have never seen one except as an extension from a mural thrombus in the left auricle or an extension from subacute bacterial endocarditis of the mitral valve.

DR. REED HARWOOD: I should like to mention the possibility of paradoxical embolism, part going through a septal defect to produce occlusion of the brachial artery.

CLINICAL DIAGNOSES

Carcinoma of lung.

Embolus of left brachial artery.

DR. JONES'S DIAGNOSES

Thrombophlebitis of legs.

Pulmonary embolism.

Acute cor pulmonale.

Bronchiogenic carcinoma?

Hypertensive heart disease.

ANATOMICAL DIAGNOSES

Adenocarcinoma of lung, right upper lobe, with metastases to bronchial, mesenteric and retroperitoneal lymph nodes, pulmonary lymphatics, liver, pleura and peritoneum.

Acute massive pulmonary embolism.

Phlebothrombosis of legs.

Subacute cor pulmonale.

Pulmonary infarct, left lower lobe.

Hemohydrothorax, right.

Hydrothorax, left.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: On opening the right pleural cavity a 1500 cc. of hemorrhagic, slightly turbid fluid was found, and scattered along the parietal pleura were numerous flecks of obvious carcinoma. The primary cancer was in the main bronchus of the right upper lobe, about 3 cm. from the carina. There were large metastatic bronchial lymph nodes, which represented the shadow seen in the right hilus. There were metastases throughout the liver, and this adequately explains the size of the liver. There were also metastases to the peritoneum and to some of the mesenteric and retroperitoneal lymph nodes. Microscopically the

tumor was a poorly differentiated adenocarcinoma. The left pleural cavity contained about 50 cc. of straw-colored fluid, and in the left lower lobe was a small hemorrhagic infarct of several days' duration. The immediate cause of death was a massive embolism to the main pulmonary artery, which apparently arose from thrombi in the deep veins of the calf of one leg. The veins of both legs were thrombosed. Most of the lymphatics throughout both lungs were plugged with carcinoma, and I believe this was the cause of the right-axis deviation. This is the second case of this condition, called "subacute cor pulmonale" by Brill and Robertson,¹ that we have recently seen.² I am sure that the infarct in the left lower lobe was not enough to have produced right-sided heart failure.

We examined the right subclavian and axillary veins and arteries but were unable to find an embolus.

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CASE 29292

PRESENTATION OF CASE

A thirty-two-year-old unmarried woman, an office worker, entered the hospital complaining of nausea and soreness in the right abdomen.

Five months prior to admission, after a brisk walk, the patient noted the onset of crampy pain in the right lower quadrant, which doubled her up and caused nausea without vomiting. For two days following the attack she had tenderness in the right lower quadrant. Her physician found a soft movable mass under the umbilicus, and marked tenderness in the right lower quadrant. The uterus was small and anteverted. In the right vault was a tender, large, thick, cystic mass. Three days later the mass had disappeared, although there was still marked tenderness, as well as a hard tender mass, in the right lower quadrant. The patient was not seen for the next four months; during that period she had several similar attacks of crampy pain, which doubled her up and forced her to go to bed. During some attacks she felt nauseated and had either diarrhea or constipation. The last menstrual period began thirteen days prior to admission, and associated with this the patient had an attack of severe pain in the right lower quadrant and lower abdomen that lasted several hours. After a three-day menstrual flow the pain disappeared and she then resumed nor-

mal activity. During the past six months the patient had lost 10 pounds.

The family history was noncontributory. The menarche occurred at fourteen; periods were regular, with a twenty-eight-day interval, and lasted three days, four or five napkins being used a day. There was moderate crampy pain in the lower abdomen during the first day, but no clots were passed and there was no leukorrhea. Menstrual cramps had increased in severity during the two years prior to admission. Six years prior to admission, at a community hospital, a uterine suspension, appendectomy and resection of an ovarian cyst were performed.

Physical examination disclosed a well-developed and well-nourished woman. The heart and lungs were normal. There was a well-healed midline scar in the lower abdomen. Deep in the right lower quadrant there was a slightly tender, fairly indefinite sausage-shaped mass. Pelvic examination revealed a small uterus and cervix. The whole right vault was occupied by a large, tender, thick-walled mass.

The blood pressure was 110 systolic, 75 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a hemoglobin of 11.6 gm. per 100 cc. The urine was normal. A blood Hinton test was negative.

An operation was performed on the second hospital day.

DIFFERENTIAL DIAGNOSIS

DR. FRANCIS INGERSOLL: It is of interest to note that this patient's pain was always on the right side, was always described as being crampy and was always associated with nausea without vomiting and that she had had increasing dysmenorrhea over a period of two years. The record does not state that the ovary was removed, so we can assume that she still had a portion of the right ovary. On physical examination there was a mass in the right lower quadrant and one in the pelvis. One cannot tell whether the same mass was felt by pelvic and abdominal examination.

This was an acute abdominal case, and it seems to me that the story of having had crampy abdominal pain with nausea makes one consider in the differential diagnosis some pathologic process that involved the gastrointestinal tract. On the other hand, since the pain seemed to come on with her periods, one must also consider a disease involving the genital tract. One might naturally assume that something was wrong with the appendix. However, since the appendix had been removed, it need not be considered in the differential diagnosis. Although it is often true that a patient is told

that the appendix has been removed when it has not, I think that we can discuss this case with the assumption that it was.

If one considers a pathologic process involving both the genital tract and the gastrointestinal tract, the first one that comes to mind is endometriosis. Cases have been reported in which the patient had endometriosis in the pelvis and endometriosis involving the bowel, usually around the sigmoid on the left side. Endometriosis may even involve the small bowel to such an extent that the patient has some degree of intestinal obstruction. So, as the first and best possibility to explain this patient's symptoms I should say that she had endometriosis, that the thick-walled cyst that was felt in the pelvis was an endometrioma, and that she also had an endometriosis that involved the small bowel. Possibly the small bowel was adherent to the endometrioma in the pelvis, and when she had her last episode of pain, which was with a period, she had bled into the endometrioma.

There are many other possibilities that should be considered. The patient might very well have had chronic pelvic inflammation. Certainly in pelvic inflammatory disease a person can have many gastrointestinal symptoms and often pain associated with periods. That might explain the symptoms, but it seems to me that with pelvic inflammatory disease the patient would not have been so comfortable, and she should have had more fever at some time during her illness. Although the episode five months prior to admission might have been the time that she had her first attack of pelvic infection, why a cystic mass was felt and later disappeared is hard to explain by pelvic inflammatory disease. This can, however, be explained by endometriosis. On the other hand, this might have been some type of bilateral ovarian cyst. Possibly the mass was an ovarian cyst that had twisted at the time of the first attack and had caused the pain after she had taken a walk. At the time she had the pelvic mass there was a mass in the right lower quadrant, so one would have to postulate that she had two ovarian cysts to account for the physical findings. One might explain the syndrome on the basis of regional enteritis, although that is just a stab in the dark. Certainly nausea and crampy pain can be caused by this disease, but one would expect some fever with it. An inflamed Meckel's diverticulum could produce a mass in the pelvis and something that could be felt in the right lower quadrant. However, the best explanation that I can offer is endometriosis, an endometrioma in the right vault to account for the gastrointestinal symptoms and endometriosis involving the small bowel.

DR. BENJAMIN CASTLEMAN: Have you anything to add, Dr. Meigs?

DR. JOE V. MEIGS: I think that Dr. Ingersoll has discussed the case exceedingly well, and I agree with him.

DR. CASTLEMAN: Perhaps you can answer the question about the umbilical mass, Dr. Simmons?

DR. FRED SIMMONS: The mass was described on the first office visit, and disappeared following a soapsuds enema three days later. I think that can rightly be termed a "red herring." I followed this woman for a month; she then disappeared and I had to write a letter to get her in again. The mass was still present, and since I could not rule out ovarian tumor, I believed that she needed exploration for that reason. Endometriosis was certainly a likely possibility.

On opening the abdomen we found an ovarian tumor on the right. The ovary was three times normal size, the upper third being replaced by a large cyst, which was believed to be endometriosis. The rest of the ovary was normal. Both tubes and ovaries were bound down by multiple, firm, dense adhesions, apparently the result of endometriosis. Adherent to the right tube and ovary was a greatly dilated ptotic type of cecum, which overlay the broad ligament and the back of the right cornu of the uterus. The rectum was adherent to the left tube and uterus. All the adhesions were broken up by sharp and blunt dissection, and the cecum was freed from the adnexa and uterus. I assumed that the first operation was for endometrioma in the right ovary and that many of the adhesions were due to the earlier operation. The patency of the right tube was demonstrated. Because the patient was thirty-two years old and because in this hospital the trend is toward conservative surgery in endometriosis for the sake of later childbearing, only the large cyst in the right ovary was resected, the uterus being suspended. She made an uneventful convalescence.

CLINICAL DIAGNOSES

Ovarian cyst.

Pelvic inflammatory disease.

DR. INGERSOLL'S DIAGNOSIS

Endometriosis of ovary, pelvis and small intestine.

ANATOMICAL DIAGNOSIS

Endometriosis of ovary and pelvis.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The ovarian cyst showed characteristic endometriosis without evidence of inflammation around it.

DR MEIGS We see a lot of endometriosis at this hospital. Do you see it at the Free Hospital for Women, Dr Rock?

DR JOHN ROCK Yes, it is a common disease.

DR MEIGS It seems to me that endometriosis is a physiologic process and occurs in almost every woman who does not have children. Perhaps that is the answer, perhaps it is not. In a large percentage of the patients I operate on, if the pelvis is examined carefully an area of endometriosis will be found.¹ It is a disease, and it is pathologic when it is far enough advanced to interfere with normal function. When I find small areas of endometriosis I consider them to be of academic interest, and remove a piece for diagnosis. The percentage of endometriosis in my operative cases must be about 40 per cent. It is a condition that occurs in women who do not have children and is usually of little significance.

DR CASTLEMAN In what percentage would you say that it does not involve the ovary?

DR MEIGS A large percentage. It is frequently found in uterosacral ligaments and on the bladder flap near its junction with the uterus.

DR CASTLEMAN Do you believe that Sampson's² theory of the pathogenesis of endometriosis is ruled out by not finding it in the ovary?

DR MEIGS Sampson's work is so good that it is hard to deny it. I have a feeling that his explanation is correct for certain cases. We had a patient recently who had both tubes shut off by inflammatory disease for ten years, yet she had endometriosis in the uterosacral region.

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A HOLMES CENTENNIAL

No prophet lacks honor, save in his own country. The centennial of Oliver Wendell Holmes's justly celebrated paper, "The Contagiousness of Puerperal Fever," published in the *New England Quarterly Journal of Medicine and Surgery* in April, 1843, was scarcely noted in Boston, though it received distinguished attention elsewhere. It was a noteworthy article, for it first introduced into America the doctrine of the infective nature of puerperal septicemia. Doctor Irving's address, published elsewhere in this issue of the *Journal*, makes honorable amends for the apparent neglect,

and pays deserved tribute to the man who dared raise his voice in the wilderness to point out the responsibility of physicians for the spread of child-bed fever.

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Vinson noted that the dysphagia usually began suddenly, often when the patient choked on a piece of solid food, the point of obstruction being high in the throat. This was followed by inability to swallow solid food, particularly meat and green vegetables, as well as difficulty in swallowing pills or capsules. Liquids and soft solids were usually well taken, and the loss of body weight was not marked. There did develop, however, a moderate

or secondary anemia, which Vinson thought was due to the quality of the food taken. In 37 of the patients the hemoglobin was 60 per cent or under. Enlargement of the spleen was noted in 12 cases in which the history of dysphagia was of long standing and the anemia, for the most part, was marked. Roentgenographic examinations in all cases gave negative results; and esophagoscopic examinations failed to reveal any lesions.

Although a plain esophageal sound was passed into the stomach in all cases, this resulted in no real stretching of the esophagus, and the effective treatment was on the basis of suggestion. This was followed by encouragement in eating solid foods and by the administration of iron and arsenic. Vinson states that the blood picture improved rapidly, the spleen returned to normal size and usually nothing further was needed to bring about an immediate, temporary cure. He found that recurrences were likely unless the patients were constantly reassured in regard to their condition. Sometimes a second passage of the sound was needed.

Vinson added that Plummer first pointed out this complex of dysphagia without organic obstruction, anemia and enlargement of the spleen. No reference, however, was given to Plummer's account, and it presumably was not published.

In the discussion of Vinson's paper, which was presented before the Minnesota State Medical Association on August 26, 1921, Dr R. Rizer, of Minneapolis, suggested that Vinson's name should be given to this disease. Another discussor did not agree with this point of view, but in spite of his opposition, the name "Plummer-Vinson Syndrome" came into the literature and has received wide recognition.

It is now known that this syndrome was described before 1922, when Vinson's paper was published. Hurst² has recently called attention to the fact that the syndrome was noted by Paterson³ at a meeting of the Laryngological Section of the Royal Society of Medicine, held on May 2, 1919. Paterson gave an even more complete description of the condition than did Vinson, for he noted

atrophy of the mucous membrane of the tongue, which is now known to accompany this condition. At the same meeting, this syndrome was also described by Kelly.⁴ He, too, noticed that in a few cases the mucous membrane of the pharynx had a pale, waxy aspect and that the tongue was smooth and devoid of papillae. Kelly attributed this appearance to the anemia resulting from the restricted and often insufficient diet. Hurst does not refer to this paper by Kelly, which seems to have equal value with that by Paterson. It is Hurst's opinion that the condition should be known as "the upper dysphagia with anemia syndrome of Paterson." To this should be added the name of Kelly. It would be even more advisable to use the term suggested by Suzman,⁵ 'the syndrome of anemia, glossitis and dysphagia'.

Hurst states that the syndrome occurs in about 15 per cent of all cases of simple achlorhydric anemia, is usually noted between the ages of thirty and fifty and is rarely found in men. It appears to be the direct result of iron deficiency due to a diet containing too little meat and green vegetables. The anemia is rapidly overcome by the administration of 30 gr. of iron and ammonium citrate three times a day. In some long standing cases, malignant degeneration has followed the atrophy of the mucous membrane.

A good many facts about this syndrome are not clear, and differentiation from allied conditions is not always possible. Strictly speaking, the dysphagia is due to a functional loss in the first stage of swallowing, in moving the food from the anterior part of the mouth back to the pharyngeal wall, where the reflex is initiated. The swallowing itself, when the bolus reaches this point, is normal, and thus the condition is not demonstrable by fluoroscopy with barium. The syndrome should therefore not be confused with many conditions that result in difficulty in swallowing in the second stage, such as constriction of the pharynx and esophagus due to scars or tumor and paralysis of the pharyngeal muscles occurring temporarily in myasthenia gravis and permanently in bulbar paralysis. There may, however, be anemic condi-

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A HOLMES CENTENNIAL

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than is necessary in the care of military casualties, for the following reasons:

The injured may include individuals of all ages and with various types of pre-existing disease, instead of a selected group of healthy young males. The possibility of toxic effects is therefore greatly enhanced. Moreover, it is assumed that in civilian injuries, hospitalization will be possible in a relatively short time, whereas in military operations such is not always the case. This usually makes it possible to postpone all consideration of chemotherapy until the injured have been hospitalized. It is then possible to administer sulfonamides with better safeguards and to consider such contraindications as other pathological conditions or known sensitivity to individual drugs. The dangers of dehydration can also be better prevented or overcome under such circumstances.

In a discussion of intra-abdominal wounds leading to perforation of the hollow viscera, the revised pamphlet advises sodium sulfadiazine as the drug of choice for parenteral administration, which is considered preferable to oral therapy during the first forty-eight hours. Sulfanilamide was recommended in the previous edition. Concentrated solutions of sodium sulfadiazine are not recommended for subcutaneous or intramuscular routes, but it is pointed out that weak (0.5 per cent) solutions may be used with little danger of sloughing of the tissues.

Special emphasis is placed on the danger of giving sulfonamide drugs to a patient who is not voiding normally (over 1000 cc per day). The pamphlet warns

Should circumstances require sulfonamide administration in the presence of inadequate urinary output the urine should be watched for evidence of renal damage and the dosage of drug adjusted so that a blood concentration, as evidenced by daily determinations, not to exceed 10 mg per 100 cc, is maintained. If further diminution of the urinary output occurs administration of the drug should be stopped immediately and fluids should be forced orally, if possible, and by means of glucose and water (5 per cent in sterile distilled water) intravenously if necessary. If anuria due to bilateral obstruction of the ureters develops, ureteral catheterization and lavage of the renal pelvis may be required.

The emergency care of burns is outlined as follows:

Whenever casualties with extensive burns can be admitted to hospitals without delay, and definitive treatment can be instituted promptly, morphine sulfate, $\frac{1}{2}$ gr., should be administered at the scene of the incident and no local therapy applied to the burned area except sterile gauze to exposed surfaces to prevent infection.

The most notable change in the OCD pamphlet is the withdrawal of the recommendation of the use of ointments or jellies containing tannic acid in the first aid treatment of burns. The new advice given is that when definitive care cannot be carried out within two hours, the patient should receive sufficient morphine to relieve pain (not less than $\frac{1}{2}$ gr., except in patients with lung and bronchial [and cerebral] damage, the very old or the very young) and the burned surfaces should be covered with sterile boric acid ointment or petrolatum over

which one or two layers of gauze of fine mesh (44) is smoothly applied. Over this dressing thick sterile gauze or sterile cotton waste is placed and the entire dressing is bandaged firmly but not tightly. Substitution of jelly containing 5 per cent sulfathiazole in water soluble base, which is supplied by the OCD Carrying Case A for mobile medical teams, is permissible.

The discussion of definitive treatment of burns has been expanded to stress the necessity for administration of large amounts of plasma.

In patients with severe burns, quantities up to 12 units or more may be required in the first twenty-four hours. To the patient in critical condition, plasma must be given rapidly (as much as 500 cc in ten minutes may be necessary) and not allowed to flow drop by drop. It must never be administered by any other than the intravenous route. Syringe injection may be used. If facilities for hematocrit determinations are available, the following general rule can be used for guidance regarding the amount of plasma required. For each point that the hematocrit is above 50 per cent cells at least 100 cc of plasma should be administered. If clinically satisfactory results are not obtained with this dosage, larger quantities should be given.

A footnote points out that rapid administration of intravenous fluids may be dangerous to cardiac patients and that the physician's judgment will have to determine the amount as well as the rate of administration in such cases.

The pamphlet describes open and closed treatment for burns. The open treatment that is now considered the treatment of choice and is especially recommended for the treatment of burns of the hands, face, feet, perineum and genitalia, consists essentially of the application of boric acid ointment or petrolatum with pressure dressings. Such dressings can often be left in place twelve or fourteen days. The closed treatment which is the tanning or eschar method, is particularly indicated in extensive flash or second-degree burns of the trunk. This method is recommended only if the following conditions are present: if not more than twenty-four hours have elapsed since the burned area has not been grossly contaminated, if strict surgical asepsis is employed in the preparation of the burned surface and if coagulation is rapidly accomplished that is, by the combined use of tannic acid and silver nitrate. The method of tanning described is the same as that given in the original edition of the pamphlet.

In the new directions additional emphasis is placed on masking of both the patient and his attendants, to minimize the danger of secondary infection.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

LAMPREY — ALICE CHESLEY LAMPREY, M.D., of Exeter, died June 30. She was in her eighty-second year.

Dr. Lamprey received her degree from Tufts College Medical School in 1900. She was a member of the New Hampshire Medical Society.

Her husband and a sister survive.

MISCELLANY

MASSACHUSETTS DEPARTMENT
OF PUBLIC HEALTHRÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS
FOR MAY, 1943

DISEASES	MAY 1943	MAY 1942	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	1	2	1
Chicken pox	1124	1763	1207
Diphtheria	4	16	11
Dog bite	1156	1335	1259
Dysentery, bacillary	12	5	5
German measles	6080	2443	259
Gonorrhea	360	321	358
Measles	6990	5320	4118
Meningitis, meningococcal	94	17	8
Meningitis, other forms	18	11	—
Meningitis, undetermined	8	1	—
Mumps	645	2017	977
Pneumonia, lobar	232	200	386
Salmonella infections	6	3	20
Scarlet fever	1949	1120	923
Syphilis	507	523	507
Tuberculosis, pulmonary	303	321	303
Tuberculosis, other forms	19	23	30
Typhoid fever	1	2	4
Undulant fever	4	1	4
Whooping cough	537	970	757

Meningococcal meningitis, while still at a figure nearly twelve times the seven-year median and still surpassing all records antedating March of this year, is dropping decidedly, with only 94 cases reported, compared with last month's 140 and the previous month's 130 cases.

Thus far, 1943 has seen scarlet fever at a notably high level. Since March, 1941, the monthly figures for this disease have been consistently higher than those of the previous year. In 1942, the increase became marked. The highest point in thirty-seven years was reached in April of the current year. During May, however, a significant drop is apparent, the monthly figure being the lowest since January. As regards distribution of cases, it is about as one would expect, in that the bulk of the cases occurred east of Worcester in the area of greatest population. Springfield, however, has had an unusual number of cases of scarlet fever, which reached a peak in March and has been dropping sharply since then.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Boston, 1; total, 1.

Anthrax was reported from: Haverhill, 1; total, 1.

Diphtheria was reported from: Fall River, 1; Lowell, 1; Melrose, 1; Somerville, 1; total, 4.

Dysentery, bacillary, was reported from: Boston, 8; Medford, 4; total, 12.

Encephalitis, infectious, was reported from: Leicester, 1; Needham, 1; Waltham, 1; total, 3.

Malaria was reported from: Camp Edwards, 1; Fort Banks, 8; Fort Devens, 2; New Bedford, 1; total, 12.

Meningitis, meningococcal, was reported from: Arlington, 1; Attleboro, 1; Auburn, 1; Bellingham, 1; Belmont, 1; Billerica, 2; Boston, 30; Bridgewater, 1; Brookline, 2; Cambridge, 2; Camp Edwards, 7; Chelsea, 2; Charlton, 1; Easthampton, 1; Fairhaven, 1; Fall River, 1; Falmouth, 1; Fort Banks, 1; Fort Devens, 2; Framingham, 1; Hanover, 1; Haverhill, 1; Holyoke, 1; Hudson, 1; Lawrence, 1; Leominster, 1; Lowell, 2; Malden, 3; Melrose, 1; Methuen, 1; Milford, 1; Milton, 1; New Bedford, 1; Newburyport, 1; Quincy, 3; Revere, 1; Rockport, 1; Somerville, 1; Spring-

field, 3; Webster, 1; Williamstown, 2; Woburn, 1; Worcester, 4; total, 94.

Meningitis, other forms, was reported from: Belmont, 1; Bourne, 1; Boston, 3; Cambridge, 1; East Bridge water, 1; Easthampton, 1; Haverhill, 1; New Bedford, 1; Newton, 1; Norwood, 1; Quincy, 1; Walpole, 1; West field, 1; Worcester, 3; total, 18.

Meningitis, undetermined, was reported from: Arlington, 1; Newton, 1; Spencer, 1; Springfield, 2; Wilming ton, 1; Worcester, 1; Wrentham, 1; total, 8.

Salmonella infections were reported from: Everett, 1; Fall River, 1; Lawrence, 2; Natick, 1; North Andover, 1; total, 6.

Septic sore throat was reported from: Boston, 7; Brook field, 1; Haverhill, 1; Merrimac, 1; total, 10.

Tetanus was reported from: Lynn, 1; total, 1.

Trachoma was reported from: Fall River, 1; Wey mouth, 1; total, 2.

Typhoid fever was reported from: Dalton, 1; total, 1.

Undulant fever was reported from: Boston, 1; Gloucester, 1; Uxbridge, 1; Williamstown, 1; total, 4.

BOOK REVIEWS

The Medals of the United States Army Medical Department and Medals Honoring Army Medical Officers. By Edgar E. Hume, M.D., D.P.H., D.T.M., LL.D. 16", paper, 169 pp., with 23 plates. New York: The American Numismatic Society, 1942. \$3.00.

Colonel Hume, a well-known historian of the Medical Department of the United States Army, has listed all the medals that have been issued honoring army medical officers. With each description of the medal itself is contained a brief note about the individual who established the gift and the man honored by the medal. There is also considerable historical information in regard to the founding of the Medical Department of the United States Army and the establishment of the Army Medical School, the Army Veterinarian School, the Medical Field Service School and other departments, including the Army School of Nursing and the School of Aviation Medicine. Each medal is illustrated.

This record is invaluable as a historical document and contains considerable material not easily available in other form. The book is a complete, carefully documented account, which should be of interest to a wide audience and should serve as a reference book in every medical library. Medical historians and librarians are greatly indebted to the American Numismatic Society for making this monograph possible.

The Answer Is . . . Your Nerves. By Arnold S. Jackson, M.D. With a chapter by The Rev. Edwin O. Kennedy. 12", cloth, 197 pp., with 10 illustrations. Madison, Wisconsin: Kilgore Printing Company, 1942. \$2.00

This is a popular account of nervous diseases as seen in a large clinic and also in private practice. The book is well written and adequately covers the field. Of particular value are the striking and often amusing illustrations that accompany the text. It is a useful, small publication, which should be widely read, both by physicians and their patients.

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DIAPHRAGMATIC (HIATUS) HERNIA*

A Clinical Study

W. RICHARD OHLER, M.D.,† AND MAX RITVO, M.D.‡

BOSTON

DURING the last thirty years there has been published an extensive literature based on the study of large series of cases dealing with the signs, symptoms and differential diagnosis of hiatus hernia. Despite this, clinicians have been slow to appreciate the full importance of the disease, especially in the differential diagnosis of certain thoracic and abdominal conditions.

Any such point of view is not without medical literature to the contrary. As early as 1853, Bowditch¹ wrote a lengthy treatise on the subject of diaphragmatic hernia and reviewed the literature. The actual number of references in the literature was twenty-seven, beginning with the first reference to the disease made by Ambroise Paré in 1610. Bowditch carefully reviewed the symptomatology of the condition, which included most of the symptoms recognized today. Following the work of Bowditch, little appeared in the American literature until 1901, when Ingals² published an article entitled "The Diagnosis of Diaphragmatic Hernia." It is of considerable interest that the author mentions the following as the principal symptoms: dyspnea on exertion and sometimes on lying down, pain in the bowel, especially after a full meal and in cases in which the opening was small, and vomiting in many cases in which the opening was large.

PATHOLOGIC ANATOMY

Most observers conclude that all cases of diaphragmatic hernia are actually or essentially congenital in origin. Polley³ suggests that age and obesity are contributing factors. He quotes other factors set forth by Akerlund as follows: stretching

of the hiatus due to insufficiency of the surrounding muscle fibers, decrease in the amount of fat tissue in the esophageal ring, decrease in the elasticity of the elastic fibrous tissue about the hiatus, loosening of the connective tissue between the esophagus and the peritoneum and increase in intra-abdominal tension. In addition, Giffin⁴ and Vinson⁵ mention trauma or minor injuries; Ritvo⁶ stresses increased abdominal tension and enumerates various causes; Turner,⁷ and also Gaudrault and Chalmers,⁸ suggest the production of hiatus hernia by increased abdominal pressure associated with neoplastic disease. Finally, Weintraub and Tuggle⁹ mention the high incidence of diaphragmatic hernia in cases of duodenal diverticulum, concluding that if one congenital defect is found in the gastrointestinal tract, others are likely to be present.

SYMPTOMS

The symptoms of hiatus hernia may simulate any one of several conditions in either the anterior chest or upper abdomen. In describing this close relation Morton¹⁰ aptly uses the term "mimic." Large series of cases have been reported by Giffin,⁴ Hedblom,¹¹ Ritvo,⁶ Dunhill,¹² Morrison,¹³ Cowan,¹⁴ Bock, Dulin and Brooke,¹⁵ Harrington,¹⁶ Dwyer,¹⁷ Moersch,¹⁸ Jenkinson and Roberts,¹⁹ Polley³ and Jones.²⁰ Harrington²¹ states that the symptoms may begin at birth or any time during life, and Ladd and Gross²² call attention to the similarity of symptoms in children with those found in adults. In general, most authors agree that symptoms are more likely to occur in middle life, for reasons already stated.

Abdominal

From a review of certain articles in the literature (Cowan,¹⁴ Hedblom¹¹ and Harrington,²³ it appears that the commonest abdominal symptoms,

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listed in order of frequency, are as follows: epigastric pain, a feeling of distress after or during a meal associated with bloating, belching and heartburn, nausea, vomiting and regurgitation, night pain or pain in the recumbent position, dysphagia and hiccough. Various methods for the relief of symptoms have been advocated, chief among which are getting up and walking about, induced vomiting, use of the stomach tube, defecation or use of enemas, alkalies and belladonna. Bock, Dulin and Brooke¹⁵ mention the feeling as if a rib had slipped in the lower left chest, especially when the patient is bending forward. Ritvo⁶ states that the most significant complaint is a feeling of weight or pressure under the xiphoid, coming on during or shortly after eating and relieved by a hot drink or by walking about for a few moments. Polley³ concludes that there is no relation between the severity of symptoms and the type or size of the hernia, and Jones²⁰ is convinced of the importance of small hernias in causing pain.

Anterior Chest

The chest symptoms of hiatus hernia are frequently similar to those of heart disease, especially angina pectoris. Many observers (Harrington,²³ Dwyer,¹⁷ Healy,²⁴ Truesdale,²³ Weitzen,²⁶ Johnson,²⁷ Jones²⁰ and Hedblom²⁸) call attention to the importance of substernal pain in hiatus hernia, and to the fact that the pain may be agonizing and may radiate to the shoulder and down the left arm. Jones finds that substernal pain is more likely to occur in patients who have small hernias. He also mentions cases with substernal pain radiating to the left shoulder down the arm into the ring finger, and also points out that exertion, nervous tension and large meals are precipitating factors. Reid²⁹ describes a case of hiatus hernia occurring in a physician that simulated cardiac infarction. The detailed report of this case, with the various suggestions made by colleagues to explain the symptoms, is both interesting and instructive. In addition to substernal pain, many observers mention dyspnea and palpitation, especially in the recumbent position or after meals. Also, McGinn and Spear³⁰ describe a patient with a large diaphragmatic hernia who had a cor pulmonale and marked dyspnea. They suggest that compression of the lungs by the herniating stomach causes an acute right-sided heart strain.

Attempts to explain the cause of chest pain in hiatus hernia reveal some difference of opinion. Johnson²⁷ suggests that the cardiorespiratory symptoms are due to the pressure of the hernial contents on the vagus nerve as it passes through the hiatus.

Gilbert, LeRoy and Fenn,³¹ as a result of animal experimental work, found that distention of the stomach or peritoneal cavity caused a decrease in the blood flow through the circumflex branch of the left coronary artery, thus explaining attacks of angina pectoris in patients with distended stomachs. Jones,²⁰ in a careful study of the mechanism of pain in both angina and hiatus hernia, concludes that overdistention of the lower end of the esophagus or the herniated portion of the stomach, with or without associated esophagitis or gastritis, may be responsible for the production of anginal pain in any or all of its components.

COMPLICATIONS

It is generally agreed by various observers that hemorrhage is the most important complication of hiatus hernia. (Giffin,⁴ Bock et al.,¹⁵ Gardner,³² Moersch,¹⁸ Eusterman and Morlock,³³ Wilkinson and Adams,³⁴ Polley³ and Jones.²⁰) Concerning the actual cause of the bleeding there is some doubt. In a case reported in the Cabot Case Records,³⁵ bleeding was supposed to have been due to varices in the blood vessels of the gastric mucosa. Also, Bock concludes as a result of post-mortem study that congestion of the mucous membrane of the stomach presumably caused by increased venous pressure is the cause of the bleeding. On the other hand, Truesdale, Hunt and Leigh³⁶ claim that hemorrhage is due to erosion or ulceration of a portion of the stomach that has become incarcerated, constricted or fixed. These authors also discussed the role of obstruction as a possible complication and, later, Truesdale³⁷ debated the problem of the development of gastric ulcer and possibly cancer. The possibility that large hernial sacs may cause right-sided heart failure has been mentioned previously.

* * *

The above review of certain articles from the literature is sufficient to demonstrate the fact that since 1912 there has been considerable interest in the subject of hiatus hernia, and that the symptomatology and differential diagnosis have been well described. However, if experience over a period of years in a large general hospital is any guide, clinicians have been slow to include this condition in the differential diagnosis of upper abdominal and anterior chest disease.

Since it has been possible to collect from the records of the Boston City Hospital a series of 128 cases during a period of less than four years, the condition is not rare. In fact, more attention to symptoms may demonstrate that the abnormality is fairly common.

ANALYSIS OF CASES

One hundred and thirty-six cases have been reviewed—128 from the hospital records and 2 from the private files of one of us (WRO). In the following tables an attempt is made to classify the various symptoms and signs, together with important complications.

Jones²⁰ classified as small those hernias that do not exceed a maximum diameter of 7 cm. In the hernias classified as large in his series, at least one third of the stomach was involved. Lacking definite information regarding measurements in our series, we have accepted the roentgenologist's

TABLE 1 Size of Hernias

Size	No.	Cx.
Small	58	
Moderately large	17	
Large (at least one third of the stomach herniated)	40	
Unclassified	39	
Total	144	

description as and when given (Table 1), being careful to speak of large hernias only when at least one third of the stomach was herniated through the hiatus opening.

Of the 136 patients with hiatus hernia, 18 were considered to have a congenitally short esophagus.

In the group of associated diagnoses (Table 2), there are a number of conditions that may give rise to symptoms similar to those of hiatus hernia.

TABLE 2 Important Associated Diagnoses

DIAGNOSIS	No. of Cases
Diverticulum of esophagus	3
Cancer of esophagus	2
Peptic ulcer	7
Cancer of stomach	4
Diverticulum of duodenum	4
Diverticulum of colon	7
Gall bladder disease, cholecystitis or cholelithiasis or both (diagnoses by x-ray or operation or both)	5
Total	32

Therefore, in the following discussion the 32 cases with important associated diagnoses are omitted, leaving a total of 104. The finding of 4 cases of diverticulum of the duodenum and 7 cases of diverticulitis of the colon is of some interest. Weintraub and Tuggle,⁹ in a study of 310 cases of duodenal diverticulum, found that 9 per cent of the patients had an associated hiatus hernia and 23 per cent an associated diverticulitis of the large bowel.

In general, symptoms fall into groups suggesting peptic ulcer, gastrointestinal malignancy, gall-bladder disease or heart disease. Realizing that an absolute differentiation cannot be made, the best

we can do is to group material according to predominant symptoms (Table 3).

Of the 9 patients without symptoms, 4 had small hernias and 5 had large hernias, with even distribution of at least two thirds of the stomach

TABLE 3 Classification according to Predominant Symptoms

SYMPTOMS	No. of Cases
Gastrointestinal	59
Gall bladder	23
Coronary	9
None	9
Total	104

Among the thirteen cases with symptoms suggesting coronary disease, one or more of the observers who saw these patients was of the opinion that 6 of the patients had definite coronary artery disease in addition to a hiatus hernia, and in one case this opinion was supported by suggestive electrocardiographic changes. Finally, it should be mentioned that in the 82 cases with symptoms suggesting either gall bladder or gastrointestinal disease, careful x-ray studies revealed no disease other than a hiatus hernia. Despite this fact, several patients in this group were unnecessarily submitted to surgery.

Table 4 lists the symptoms in 95 cases, regardless of the size of the hernia. An attempt was made to classify symptoms according to the size of the lesion but without clear cut differential data. It is to be remembered that hernial size may

TABLE 4 Distribution of Symptoms (95 Cases)

SYMPTOMS	No. of Cases
Epigastric pain or distress (shortly after meals generally associated with sense of fullness)	52
Rad at on to mid back	4
Rad ation to shoulders	5
Nausea or vomiting or both	44
Heartburn	22
Belching	21
Night pain	16
Difficulty in swallowing	14
Weight loss	18
Loss of appetite	12
Dyspnea	7
Hiccough	3
Substernal pain	24
To right of sternum	2
To left of sternum	5
Rad at on to mid back	5
Rad ation to left shoulder	4
Rad ation to left arm	1
Increased by exertion	4
Unrelated to exertion	5

change from time to time and that a single observation by x-ray is not necessarily an accurate basis for a definite classification. At any rate, in the 13 cases with symptoms suggesting coronary disease, 5 patients had large, 2 moderately large, and 6 small hernias.

The symptoms in 95 cases were relieved as follows: by assuming the upright position, 13 cases; by the use of soda, 11 cases; by vomiting, 6 cases; by belching and by lying down, 3 cases each; and by defecation, 2 cases.

Among the 104 cases, there were 29 cases with mild hemorrhage, and 12 with gross bleeding. Only those cases are included that revealed an appreciable fall in hemoglobin level and red-cell count and at least a ++ guaiac test for occult blood in the stools. Cases listed as having had a gross hemorrhage include only those with a hemoglobin level of 50 per cent or lower. Consideration of hemorrhage in relation to the size of the hernia is of interest (Table 5). Of real impor-

to endanger life. Finally, it appears from this study — although definite proof is lacking owing to insufficient data — that symptoms and complications are not related to the size of the hernia.

Such is a composite clinical picture of a patient with hiatus hernia as drawn from the records of the Boston City Hospital. In general, this picture corresponds with the many found in the medical literature.

X-RAY DIAGNOSIS

Since the manifestations of hiatus hernia are so variable and inconstant that clinical diagnosis is usually impossible, x-ray demonstration is necessary to establish the presence of the abnormality. In some patients routine x-ray studies of the esophagus and stomach suffice to outline the hernia. In the majority of cases, however, the lesion is very small or for other reasons difficult to visualize. In these cases it may require the utmost care on the part of the roentgenologist to prove the existence of the hernia.

In searching for an esophageal hiatus hernia, the x-ray examination should always begin with fluoroscopic observations without the opaque meal. A careful and thorough search is made for a gas-containing shadow lying at or slightly above the level of the diaphragm. This is of particular importance since in some cases the hernia reduces itself and disappears on ingestion of the opaque meal. Observations are first made with the patient breathing quietly, then in full inspiration and forced expiration. The frontal and oblique positions are used in the erect, prone and supine positions. Occasionally both gas and fluid are present within the herniated portion of the stomach, presenting a horizontal fluid level with an air bubble above the liquid.

When the opaque meal is administered, the fluoroscopic observations are best begun with the patient in the erect position. Each mouthful is carefully observed in its passage through the esophagus. The lower end of the esophagus may be tortuous and moderately dilated. Rarely, pressure of the hernia produces esophageal obstruction, with consequent dilatation. In patients with congenital shortening of the esophagus, the cardioesophageal junction is seen to be above the level of the diaphragm. The hernia in many cases fills partially or completely with the patient erect. However, it has been our experience that the great majority of hernias are not demonstrable in this position. Therefore, if the x-ray observations are carried out only with the patient upright, as is the case in some clinics, a large percentage of the lesions will not be visualized and the diagnosis will consequently be missed.

TABLE 5. Hemorrhage in Relation to Size of Hernia.

SIZE OF HERNIA	TOTAL NO. OF CASES	CASES WITH MILD HEMORRHAGE	CASES WITH GROSS HEMORRHAGE
Small	43	12	4
Moderately large....	10	2	3
Large	27	9	1
Unclassified	24	6	4
Totals	104	29	12

tance, however, is the observation that bleeding of either mild or severe type is just as likely to occur regardless of the size of the hernia.

SUMMARY OF CLINICAL DATA

The typical symptom of hiatus hernia may be described as a sense of epigastric pain, distress and fullness coming on shortly after or during meals. Frequently this symptom is associated with nausea, vomiting, regurgitation, belching or a sense of burning, but not infrequently these symptoms are independent. Often there is difficulty in swallowing solid food, lack of appetite and associated weight loss. Very frequently there is epigastric pain or distress appearing at night or when the patient is in the recumbent position, but in most cases this pain is relieved when the patient assumes the upright position. For the digestive symptoms mentioned above, change in position may bring relief, but just as frequently soda gives relief, and occasionally a patient complains of inability to raise gas. There is often substernal pain or dyspnea or both — generally but not always unrelated to exertion. The pain may present a type of radiation similar to that of angina pectoris, but just as frequently its radiation is atypical. Furthermore, the patient with hiatus hernia may bleed. The bleeding may be of mild degree, in which event it may well explain the finding of anemia characteristic of chronic blood loss, or the patient may have a hemorrhage sufficiently severe

It is with the patient lying down that the hernia is most apt to be demonstrated and its size and shape best outlined. Deep, forced breathing, pressure on the abdomen, lowering the head of the table, filling the colon with barium or air, asking the patient to strain or cough—these or other maneuvers that tend to increase the intra-abdominal tension may be used to help visualize the hernia. Complete filling of the stomach with the barium meal is important. The patient must be observed in the prone, supine and oblique positions, no one position being optimum for all cases.

Although fluoroscopic observations usually serve better than x-ray films for the demonstration of the hernia, the latter should be made in every case. Occasionally the lesion is visualized only in the films and not during fluoroscopy. Spot films exposed during roentgenoscopy are now available in most clinics and are extremely helpful in the study of difficult cases. The hernia appears as a rounded or oval shadow in the posteromedial portion of the thoracic cavity just above the diaphragm. Rugal folds are demonstrable in the herniated portion of the stomach, extending through the esophageal orifice of the diaphragm. The size and shape of the hernia vary widely in different patients, and in the same patient at various times. Small lesions may be but a few millimeters in diameter; the largest may comprise half or more of the stomach. The hernia most commonly lies to the left of and anteriorly to the esophagus. With large hernias the esophagus may appear to be encircled by the herniated portion of the stomach. Cancer or ulcer may occur in the hernia or other parts of the stomach, and a careful search for other pathologic processes should be made in every case.

TREATMENT

Hiatus hernia may present no symptoms and therefore require no treatment. All observers are agreed that treatment is essentially medical, especially in patients with small lesions. A bland, high-vitamin diet, divided into four or six feedings, is desirable. Food should not be given before bedtime. Assumption of the upright position after eating or for a few minutes during the course of the meal is often helpful. In many cases sleeping at an angle of 45° has relieved distressing night symptoms. Various alkalies and antispasmodic drugs are frequently useful. Recently Levy and Duggan²⁸ have emphasized the psychic factor in the management of such cases. Surgery is indicated when medical measures fail to give relief, especially in patients having intractable pain or hemorrhagic tendencies. A large measure of relief may result from interruption of the left phrenic

nerve. On the other hand, surgical repair offers a complete cure, and the surgical technic of the procedure has been well standardized.

In our series, 4 patients had phrenic-nerve interruption and 1 was operated on for repair of the hernia, in all cases because of attacks of severe epigastric pain. In the 4 cases in which the phrenic nerve was interrupted, relief was either partial or temporary. In the single case of hernia repair, relief was permanent.

DISCUSSION

It is generally believed that hiatus hernia is congenital. It must follow that most patients have the condition for many years before exhibiting symptoms. Actually, in most cases, symptoms come at a period in life when one may expect the onset of symptoms of other conditions, all of which serve to complicate the study. The symptomatology and clinical findings of hiatus hernia are inconstant and variable, so that although the existence of the condition may be suspected by the clinician, it is usually impossible to make the diagnosis with certainty on the basis of the history and physical examination alone. Furthermore, many of the complaints in hiatus hernia are also present in other, commoner diseases. It is highly desirable, therefore, to establish a syndrome on which a definite diagnosis is tenable.

In obtaining detailed histories of a large series of cases, a group of symptoms that have been met in a small number of patients but that have proved extremely significant are the following: a feeling of fullness, pain or distress in the epigastrium or under the tip of the xiphoid, coming on with the ingestion of the first few mouthfuls of food. In some cases these symptoms are so severe that they necessitate the interruption of the meal. However, on leaving the table and walking about for a short time, the patient may experience a sudden disappearance of the complaints, often with a feeling of something dropping or giving way in the region of the lower sternum. He is then able to return and finish the meal in entire comfort. The explanation is doubtless that the food first ingested produces filling of the herniated portion of the stomach, with distortion, compression and complete or partial obstruction of the esophagus; on arising and moving about, the herniated portion of the stomach empties or reduces itself, with resultant disappearance of the symptoms. In the experience of one of us (M.R.), this is pathognomonic of hiatus hernia, and although it occurs in relatively few cases, permits a practically definite diagnosis. Rarely, patients with

cardiospasm or esophageal diverticulum may give a somewhat similar history. In these conditions, however, the relief is usually not produced by arising and walking about, nor is it so immediate and complete.

Inasmuch as the clinical picture of hiatus hernia is similar to that of other disease in the chest or abdomen, one must be entirely certain of the state of affairs before assuming that hiatus hernia is the only cause of existing trouble. Recently we have seen a case of hiatus hernia with severe gastrointestinal bleeding in which the first gastrointestinal x-ray examination revealed no disease other than the hernia. A repeated x-ray study, however, revealed a deep duodenal ulcer in addition to the hernia. The problem becomes all the more difficult when one tries to explain attacks of chest pain on this basis. Certainly a patient may have both coronary-artery disease and a hiatus hernia. It is only after very careful study and observation, therefore, that a single diagnosis is tenable. The possibility of hiatus hernia should never be forgotten, and its presence never overlooked. Nevertheless, in one's enthusiasm at finding an abnormality that can be demonstrated, one should not neglect the fact that other disease may be present the existence of which can be demonstrated only by continued study and observation.

SUMMARY

Hiatus hernia is sufficiently common and the symptoms are such as to justify its inclusion in the differential diagnosis of anterior chest or upper abdominal complaints or both.

The presence of hiatus hernia should never be overlooked, regardless of its size.

In any case of unexplained bleeding, the presence of hiatus hernia should always be considered, since bleeding may occur in any type of case.

The symptoms of hiatus hernia may simulate those of coronary-artery disease. The differential diagnosis here is a matter of careful clinical judgment after all the data have been assembled.

A clinical syndrome pathognomonic for hiatus hernia has been suggested.

A method for determining the presence of hiatus hernia by roentgenologic examination is presented.

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PANEL DISCUSSION: CURRENT EPIDEMIC RESPIRATORY DISEASES IN CHILDREN*

CHAIRMAN'S INTRODUCTORY REMARKS

DR. CHESTER S. KEEFFER, Boston: I need not tell an audience of this kind that the respiratory infections are by far the most important group of illnesses that we deal with in medical practice. One sees them every day, and they always raise important and frequently distressing problems. We know that the respiratory infections are responsible for more disabling illness, for more absenteeism from school and from industry, than any other single group of disorders. Dr. Sisson has already referred to the fact that great strides have been made in treatment in the last few years, but very few advances have been made in prevention. So tonight the speakers are going to confine their remarks, in the main, to the treatment of these respiratory infections that are encountered every day.

ACUTE LARYNGOTRACHEOBRONCHITIS IN CHILDREN

JOHN A. V. DAVIES, M.D.†

BOSTON

I HAVE been asked to discuss what may safely be called a pediatric emergency. As you know, in past years acute laryngotracheobronchitis has carried a mortality of anywhere from 50 to 100 per cent.

When a physician is called in the dead of the night by a mother who says her infant has croup, the chances are that he has croup, and probably one is justified, after questioning her, in telling her to put the child in a room with warm steam and to give some suitable expectorant. However, it is important to bear in mind at the very outset that what seems to be a simple case of croup may actually be the start of something far more serious, that is, acute laryngotracheobronchitis.

One other disease that we see infrequently nowadays, diphtheria, should of course be borne in mind at the same time. But spasmodic croup usually follows a mild respiratory illness, most often begins at night, after perhaps a day out in the cold air, and as a rule quickly responds to steam and suitable doses of ipecac. The mother

should be warned that if the child does not respond in one or two hours, she should notify you at once, and you should examine the child carefully.

At the outset, it is often difficult to differentiate these conditions. However, acute laryngotracheobronchitis may usually be distinguished

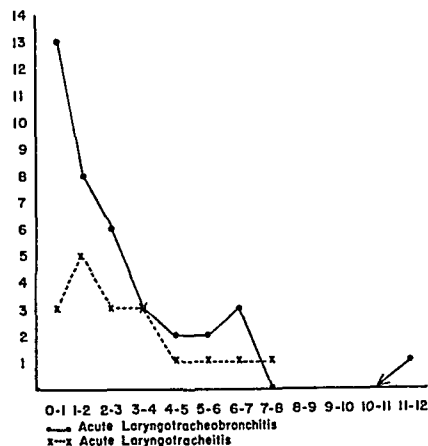


FIGURE 1. Age Incidence in 38 Cases of Laryngotracheobronchitis and 18 Cases of Laryngotracheitis.

Of the former patients, 21, and of the latter, 8 were under two years of age.

from simpler and milder forms of respiratory illness by the fact that the symptoms are progressive and persistent. The child seems sicker. There is fever, and leukocytosis also. Therefore, if the symptoms do not respond quickly to steam and an expectorant, it is obvious that additional measures should be taken to deal with this threatening situation, and there is no doubt that the hospital is the place for such a child.

Before speaking more specifically of therapy, I should like to remind you of the pathology of the disease. One is not dealing with a simple laryngitis, nor with a simple tracheal irritation. As the name implies, the inflammation extends from the throat down to the bronchi, and possibly to the bronchioles. In the early stage of the

*Presented at a meeting of the New England Pediatric Society held on March 24, 1943, at Longwood Towers, Brookline, Massachusetts.

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disease, one encounters inflammation and marked swelling of all these tissues, so that the airway is restricted. Later on, if the disease progresses, and especially if certain organisms of which I shall

TABLE 1. *Bacteria Recovered on Repeated Cultures in 33 of 38 Cases of Laryngotracheobronchitis.*

ORGANISM	NO OF CASES	PER CENT
Pure cultures	15	45
Beta hemolytic streptococcus	8	24
<i>Staph aureus</i>	4	12
Pneumococcus	3	9
Mixed cultures		
Above organisms (various combinations) and <i>H influenzae</i>	12	37
Negative cultures	6	18

speak in a moment are present, necrosis and sloughing of the membrane and plugging of the bronchi may develop with resultant atelectasis and emphysema, and possibly pneumonia. The process

throat culture was taken,—not only in the trachea and the lungs but also in the blood stream. I have emphasized the bacteriology because the tendency nowadays is to treat specific organisms in a specific way.

Standard treatment at the Children's Hospital involves teamwork between the physicians, the nursing staff and the laboratory. We have decided that the hot steam room is not so good as a room in which we have a cold humidifier and in which the temperature is kept at a level of approximately 70 to 75°F. We think that the hot room is uncomfortable to the patient and to the attendant as well. We avoid unnecessary examinations and treatments. However, we believe that it is important, having placed a child in this humidified room, to obtain the proper cultures from the throat or trachea. We also like to get a blood culture, because now and then the invading organisms are more clearly identified by this method. However,

TABLE 2. *Bacteriology in Cases of Laryngotracheobronchitis according to Age.*

ORGANISM	UNDER 2 YEARS			OVER 2 YEARS			ALL CASES	
	PURE CULTURE	MIXED CULTURE	TOTAL	PURE CULTURE	MIXED CULTURE	TOTAL	NO	PER CENT
Beta hemolytic streptococcus	2	5	7	6	2	8	15	45
<i>Staph aureus</i>	4	10	14	0	1	1	15	45
Pneumococcus	1	4	5	2	0	2	7	21
<i>H. influenzae</i>	0	3	3	0	1	1	4	12

is widespread, and no one portion of the respiratory tract is involved.

Figure 1* will remind you of the age incidence of this disease, showing that in the majority of cases the disease occurs during the first two years. Indeed, almost 50 per cent of the patients are two years of age and under.

Table 1 shows the bacteria that invade the respiratory tract. I show this because there has been a tendency to consider the beta-hemolytic streptococcus as the only organism involved, whereas *Staphylococcus aureus* and the pneumococcus are also frequently present, as well as *Haemophilus influenzae*. Table 2 is even more illuminating. In patients under two years of age, the staphylococcus is more frequently found in pure culture than is the streptococcus; after that, the streptococcus appears more important. From Table 3 it is apparent that among the autopsied cases *Staph. aureus* was also important, and that in all the fatal cases the children were under two years of age. The streptococcus and the pneumococcus were also recovered, but the staphylococcus appeared in every case,—except one in which only a

undue measures are not taken to obtain these cultures, especially when the child is precariously near the borderline between life and death. From this point on, the procedure is largely a matter of the skill and judgment of the attending physician.

On the way to the hospital, if an ambulance is employed, it is well to make sure that one has some oxygen at hand. In case the child's airway becomes completely blocked off, which sometimes happens when a child is taken from the warm home out into the winter air, a life may be saved if the accompanying physician inserts a Mosher tube into the trachea.

Having made the decision to bring the child to the hospital, it is important to put a capable laryngologist on the alert and tell him he may be called to do something for the child. What he does depends a good deal on his experience and the progress of the patient. From observation of the course of events at the Children's Hospital, I believe that in most cases tracheotomy is probably the operation of choice, if operation is necessary. It usually provides permanent relief from high obstruction. It enables one to insert a catheter and aspirate the pus and some of the exudate from the upper bronchi and lower trachea.

*For Figure 1 and Tables 1, 2 and 3 I am indebted to Dr Charles H Cutler and Dr Charles F Ferguson

On the other hand, the intubation tube tends to cause necrosis of the larynx and trachea and is sometimes coughed out, leaving the child in the condition in which he began.

I emphasized the bacteriology of the disease because we now have the assistance of the sulfonamides.

TABLE 3 Bacteriology of Fatal Cases

CASE No.	AGE	ORGANISMS	SOURCE	DAY OF ILLNESS CALCULATED	REMARKS
<i>ma</i>					
19	15	Pneumococcus (Type 23) and <i>Staph aureus</i>	Trachea and lung*	1	
		Pneumococcus (Type 23)	Blood*	1	
21	12	Beta hemolytic streptococcus	Throat	3	No autopsy
25	12	<i>Staph aureus</i>	Trachea	2	
		<i>Staph aureus</i>	Trachea	3	
		<i>Staph aureus</i>	Trachea, lung and blood*	4	
28	19	<i>Staph aureus</i>	Trachea	1	No autopsy
30	10	Pneumococcus and <i>Staph aureus</i>	Throat	2	
		<i>Staph aureus</i>	Bronchus, lung and blood*	4	
36	14	<i>Staph aureus</i>	Throat	2	
		<i>Staph aureus</i> and pneumococcus (Type 23)	Trachea	2	
		<i>Staph aureus</i>	Trachea and blood*	3	
38	12	<i>Staph aureus</i>	Trachea	2	No autopsy
		Beta hemolytic streptococcus	Trachea	9	
		Beta hemolytic streptococcus	Trachea	14	
45	13	Beta hemolytic streptococcus	Throat	2	No autopsy
		<i>Staph aureus</i>	Trachea	3	
50	15	Beta hemolytic streptococcus	Larynx	2	
		Beta hemolytic streptococcus and <i>Staph aureus</i>	Blood*	5	

*Clotted at autopsy

midex and penicillin. Since one is dealing with different organisms, not exclusively with the streptococcus, sulfathiazole or sulfadiazine may well be started on the way to the hospital. At present, penicillin is not available for general use. The dosage of the sulfonamides will be discussed later, but it should be emphasized that a full dose should be given early.

Oxygen administration is probably elective in some cases, although it should be used when cyanosis is present. It may be necessary to give it by nasal catheter. If infants under two years of age do not respond in a reasonable time to sulfonamide therapy and general supportive measures, a transfusion of blood from an adult donor should be considered, in the hope of providing certain unknown factors that the infant does not have and

that some adult may possess. Transfusions seem to help some infants with staphylococcal infections.

The question arises whether one should give other drugs, such as ipecac. I should say, No. Morphine and atropine are absolutely contraindicated, since morphine suppresses the respiratory effort, and atropine dries the secretions, already too tenacious, and thus tends to plug off the respiratory tract.

A last point concerns fluids. We try to give fluids in moderate amounts, by mouth, even after tracheotomy. If the child's condition is too bad, we give them subcutaneously. It is important, however, to remember that in a situation like this one should avoid flooding the patient with fluids because the respiratory tract is already seriously embarrassed and adding a great deal of fluid to the circulation may increase the edema fluid in the bronchi and bronchioles and cancel all that has been gained by the previous treatment.

THE DIAGNOSIS OF VIRUS AND BACTERIAL PNEUMONIA IN CHILDREN

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BOSTON

THE TERM usually applied to acute infection of the lung, other than lobar pneumonia, is "atypical pneumonia." If I were to enumerate the various terms that have been introduced in recent years as synonyms for or forms of atypical pneumonia, my time would be up before I finished. In general, the term "virus pneumonia" is loosely used to express the desire of the physician to approach an etiologic diagnosis that he cannot make.

I shall mention briefly some of the problems involved before one can rule out a definite etiologic agent, and then some of the known agents other than bacteria that may cause pneumonia. This will still leave a residue, which is bothering most of us more, perhaps, than those cases in which the etiology can be determined.

In the first place, atypical pneumonias are the ones predominating among infants, even when the causative organism is one which in older people produces lobar pneumonia, namely the pneumococcus. All other organisms produce atypical pneumonias, even in adults. Thus we have atypical pneumonias due to all bacterial agents in infants, and to all bacterial agents other than pneumococcus in young children, in whom the pneumococcus produces typical lobar consolidation.

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Pediatricians are only too well aware of the difficulties in arriving at an etiologic diagnosis in infants. First is the problem of obtaining proper materials for culture. Then again, multiple organisms are usually isolated from the nasopharynx or sputum in infants, and one is confronted with the difficulty of arriving at a conclusion concerning which of the organisms is actually causing the disease. Nowadays, the direct observations afforded by the Neufeld typing of pneumococci are of great assistance. Cultures of the material that is aspirated or is taken on a swab after encouraging a child to cough can frequently give a predominant organism, and this can usually be considered as the etiologic agent. Blood cultures are most helpful in bacterial infections.

It must be remembered that besides the pneumococcus, the staphylococcus is an important etiologic agent, especially in infants, in whom aspiration of upper respiratory contents is an important factor. The streptococcus is one of the foremost causes of the pneumonias that follow virus infections, such as measles. It is also found in the pneumonias that occur after whooping cough, and after other streptococcal infections, like scarlet fever, tonsillitis and septic sore throat.

The pneumonia produced by the streptococcus is characterized in infants and in young children by a severe type of illness that advances rapidly and is accompanied by a rapid accumulation of fluid in the chest and by extreme toxemia.

Staphylococcal infection of the lung is characterized by an insidious onset of a severe illness. There is a purulent or perhaps pinkish sputum representing an admixture of pus and blood. There is usually a severe tracheobronchitis. The course of the disease is characterized by multiple cavities in the lung, and the tendency in young children to produce abscesses that rupture into the pleura, giving rise to pyopneumothorax. Staphylococcal pneumonias occur most frequently after influenza or following aspiration in debilitated infants and children.

The influenza bacillus may cause severe infections in the lung, particularly during epidemics of clinical influenza. It is also characterized by a lesion in the trachea and bronchi and by a hemorrhagic type of bronchopneumonia that is sometimes seen in the fulminating form of a staphylococcal pneumonia.

In infants, the factor of inhalation of foreign substances, including their own upper-respiratory secretions, is important in establishing lesions in the lower respiratory tract. Foreign bodies producing or predisposing to severe and recurrent pneumonias must always be borne in mind. Any

of the common pyogenic bacteria can cause pneumonia under proper circumstances.

Of the nonbacterial agents, the commonest is the *virus of influenza*, which is capable of producing various lesions in the lung. It may also predispose to severe bacterial infections, particularly with the staphylococcus or influenza bacillus, and sometimes with other organisms, such as the streptococcus. The latter is likely to produce the post-influenzal pneumonias if streptococcal infection happens to be prevalent, or in wards where streptococcal infections occur. The pneumonia would then be characteristic of the streptococcal type.

The psittacosis virus produces a disease in human beings almost exclusively after contact with exotic birds. Recently a good deal of attention has been focused on this virus and other closely related viruses that occur in many species of birds, including certain domestic birds, such as street pigeons and domestic fowl. The disease caused by these viruses is termed "ornithosis." These agents are extremely interesting and have other relatives in the virus family, many of which, under certain circumstances, may produce pulmonary lesions and others of which are not known to produce pulmonary lesions. The diagnosis of psittacosis or ornithosis in the absence of a history of definite contact with birds is difficult. Even with such a history the diagnosis is sometimes questionable, because of the wide variety of strains that can give immunologic reactions with these related viruses.

A number of other viruses have been isolated from cases of atypical pneumonia, mostly in adults. Presumably similar cases occur in infants and young children, since there are many reports of their occurrence in small outbreaks among adolescents. One group of these viruses produces pneumonia and meningitis in mice and has been called "meningopneumonitis." Another virus has been isolated by inoculating material from human beings into cotton rats. Still another virus can be isolated only by inoculation of the mongoose, a rodent that is native to Jamaica and is not available in this country.

There are many other viruses, one of which occurs in mice, that are also closely related to the viruses of psittacosis and meningopneumonitis. A virus has been recently described that has been transmitted from kittens to human beings; this virus produces a characteristic pneumonia in young kittens, but not in adult cats.

There are other possibilities. There is Q fever, which in America has been shown to be the cause of endemic cases as well as small outbreaks of pneumonia. In Australia the agent of Q fever

produces a disease simulating influenza, and it has not been recognized as producing pneumonia there. The agent is presumably identical with that of American Q fever, both are rickettsias.

In addition to these viruses, there are others that may also be associated with lesions in the lung, presumably due to these nonbacterial agents. For example, epidemic typhus fever and South African tick fever are known to give pulmonary lesions that are similar to the pneumonias produced by other viruses. Lymphocytic choriomeningitis may also do this.

The important point is that after one tries to identify the etiologic agent with all those I have mentioned, one has identified only a small proportion of the pneumonias that are not due to bacteria. In general, the recent tendency has been to make a diagnosis of virus pneumonia when a person has been treated with a sulfonamide drug and fails to respond to it. However, one must remember two things. In the first place, even the common bacteria that are known to respond are sometimes resistant to the action of sulfonamide drugs. This is occasionally true of the pneumococcus, but resistance of pneumococcal pneumonia to sulfonamide therapy cannot be said to be a common phenomenon. Secondly, it is to be remembered that pneumonia due to organisms like the streptococcus and staphylococcus requires prolonged and intensive treatment. Thus, if one starts out with a mild infection that one is trying to treat with small doses, and the patient becomes suddenly severely ill, one may assume that one is dealing with a virus pneumonia that has not responded, when actually one is dealing with a severe staphylococcal or streptococcal pneumonia that has been inadequately treated.

There are other diseases, particularly of infants that are suspected of being of virus etiology owing to the pathological picture. There was an epidemic disease among the newborn in Minnesota in which intracellular inclusions have been demonstrated both in the lung specimens and in materials obtained from the throat. It is also true that if one examines the lungs of children who die of whooping cough, a large percentage of them have intranuclear inclusions in the epithelium of the bronchi. What relation these inclusion bodies have to the etiology of whooping cough on the one hand, or to the pneumonia of which the infants die on the other, is not altogether clear.

There are other conditions from which infants die, as, for example, malnutrition and other debilitating diseases, in which intracellular or intranuclear inclusions, or both, are found at autopsy. The relation to the fatal illness or to the pneumonia that may be present is difficult to evaluate in such cases.

THE USE OF SULFONAMIDES IN THE TREATMENT OF RESPIRATORY INFECTIONS IN CHILDREN

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THE chemotherapy of the common respiratory diseases of children presents many difficulties that one does not encounter in dealing with adults. One hears quite frequently somewhat intolerant remarks concerning practitioners who use sulfonamide drugs indiscriminately. I think that all those who do much work with the sulfonamides feel strongly against the indiscriminate use of the drugs, but in my brief few months in pediatrics, I can sympathize most heartily with those whose job it is to see children in the home and to decide with what types of infection they are dealing.

The last speaker, who probably knows as much about this subject as anyone in the field, has shown us how complex the problem has become. The job of the person seeing a sick child in weedling out the various etiologic agents is often extremely difficult, and one can hardly blame doctors for using these drugs almost indiscriminately, since in many cases they are effective. However, I consider that a defeatist attitude, and one that should not be encouraged, because there are definite indications and contraindications for their use. Children and adults got well before the days of chemotherapy. One should not let enthusiasm for a new therapeutic agent run away with one every time a person becomes ill.

What are the indications? They boil down to evidence of an acute bacterial infection of the respiratory tract that is obviously spreading and is a serious or potentially serious one.

We know that respiratory infections are due to two types of agents in general, and frequently the two agents act together. On the one hand are the viruses, on the other are the bacteria. One can make a fairly good generalization of the respiratory diseases, namely, that the sulfonamides are fairly effective against almost all the bacteria that cause respiratory infections, with the possible exception of the staphylococcus. Nevertheless they are singularly ineffective against the virus agents that often give the way for the bacterial infections, or may be the sole cause of the infection.

Therefore, anyone using the sulfonamides should try to bear in mind this question, What are the bacterial infections of the respiratory tract? And this, also, should be borne in mind. If the child shows by his clinical picture that he is suffering from a bacterial infection, how serious is that

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infection? For every bacterial infection does not need to be treated with a sulfonamide: only those that are actually serious or potentially serious require it.

What signs does one have? Perhaps the first that is of considerable help is gained by just looking at the child. How sick is the child? For example, an ordinary cold may make a child extremely uncomfortable. He may have an obstructed nose, or a cough and he may be hoarse and have a little croup; but he is not apt to have a temperature of 104 or 105°F. and be prostrated, with a marked diarrhea, vomiting or other signs of general toxicity. One cannot get away from the fact that the person who can use the sulfonamides wisely is the best doctor. One cannot lay down rules for the use of these therapeutic agents that will work for an automaton. One has to use judgment. Therefore, the first question is, How sick, really, is the child? Secondly, are there any signs of invasion? Bacteria that are localized are no great menace. It is the bacterial infection that spreads that menaces the child.

The spread in the respiratory tract is easily seen. The infection first spreads to the sinuses, which become tender and fail to transilluminate. Then there are the ears, the commonest site of all. The patient develops an acute otitis media, possibly with swelling of the mastoid process, and mastoid tenderness. A site equally common is that of the lymph nodes that drain the area. If these become swollen and tender and increase visibly in size, obviously there is an infection spreading beyond the ordinary bounds of the upper respiratory tract. The lungs, again, are a site of spreading infection. However, as already pointed out, invasion of the lungs may be purely of a virus nature.

Regarding general signs, fever, general toxicity and leukocytosis are gauges both of the severity of the illness and at times of its nature. Unfortunately children, as I have learned to my distress in the last few months, do strange things, whereas adults react more regularly. As a generalization, to which many exceptions may be taken, the virus infections of the respiratory tract are accompanied by a real leukopenia. The white-cell count, in the face of a fever, fails to go up, and even goes down. On the other hand, bacterial infection may produce a queer reaction in the bone marrow, associated with a fall in the white-cell count instead of the usual rise, which when present is a helpful sign of bacterial infection.

Having considered all these things, one admits that the child is very sick but does not know what is the matter with him, except that he has an infection of the respiratory tract. He has a cough

and the eardrums are a little injected; the throat is red, and the temperature is 104°F.; he is prostrated, vomiting and refusing food, and he is fussy. I think that under those circumstances anyone would be foolish to suppose that he runs a greater risk by giving the child the sulfonamides than by failing to do so. My own philosophy is to take the bull by the horns. If I were worried about the patient, I should go ahead and give the sulfonamides a trial. In about two or three days one will be able to determine whether any effect has been produced. If one undertakes to give the child a trial of chemotherapy, he should be sure to give the child enough drug so that it will mean something. Chemotherapy should, in my belief, either be fairly intensive or should not be employed at all. A little chemotherapy for a doubtful situation is one of the worst abuses to which the sulfonamides have been subjected. It does the patient no good and the physician is up in the air at the end of three days, not knowing whether the child is sick from the sulfonamides or from the infection, or whether the sulfonamides have done him any good. He is about three days worse off than before he started.

What are the complications associated with the use of the sulfonamides? First, there are the toxic reactions to the drug, for which the child has to be watched closely. Secondly, there is the possibility that the child may become sensitized and thus will be in for trouble when he subsequently needs the drug for a much more serious infection in the future.

What does one have to watch in the child to whom one gives chemotherapy? If it is given fairly intensively and early, and as soon as the infection is brought into control the dosage is lowered, the toxic reactions one has to fear most are those involving the kidneys. A child's urine should be examined for the presence of red cells, indicating damage to the kidneys, and the mother should be instructed to try to get some idea of how frequently the child is voiding. The blood has to be watched to a certain extent. Hemolytic reactions are rare with the new sulfonamides. Depression of the bone marrow with agranulocytosis usually does not develop until after ten to fourteen days of chemotherapy. Sensitization with fever and rash is most apt to occur in the second week. One's idea should be to treat the child intensively in the beginning, and get him off chemotherapy, if possible, before serious toxic reactions are likely to occur.

What should be done before chemotherapy is started? I should like to re-emphasize the fact that, although cultures are not always possible in the home, bacteriologic study of infections is just

as much a part of the study of the infected child as listening to the chest or looking down the throat. Certainly, in any seriously ill child or adult, the best cultures that can be obtained should be taken before chemotherapy is instituted, not because it may be impossible to get positive cultures after several days of therapy, but because by that time it may be important to know in a short space of time what the infecting organism is. If one has to wait twenty-four hours for the laboratory report, when a child is desperately ill, a family may result. Knowing what type of infection is present puts one in a relatively strong position. One has all the facts, as best he can get them. The cultures may not be too satisfactory, but at least one has made an effort. The blood culture in any seriously sick, hospitalized child should be taken, if it is humanly possible.

What drugs can be used? Obviously, sulfadiazine is the most satisfactory of the sulfonamide drugs, it disturbs the child, as well as adults, much less in every way. Its sodium salt can be given parenterally with great ease, and therefore is the ideal drug. However, one might as well be forewarned. It may not be possible to buy sulfadiazine much longer—it is just one of the short ages, like butter and coffee, that we may have to get used to. It should be remembered that all the infections that respond to sulfadiazine respond to sulfathiazole. It is my practice in urinary tract infections, which are out of the field of this discussion, to use sulfathiazole. That means that one does not use sulfadiazine for everything, and thus can save it for the serious conditions, which are usually the respiratory diseases.

Sulfathiazole can be used in the same doses as sulfadiazine, with the single exception that one must remember that sulfathiazole is much more rapidly excreted, and thus it is more difficult to maintain an adequate concentration in the child by its parenteral use without getting renal complications.

Finally, there is the question of how much to give. I should like to re-emphasize a single point: do not give chemotherapy until you have made up your mind, on the basis of what you see, whether or not the child has a severe infection. If so, use it. And use enough. That does not mean too much. We have had the pendulum swing both ways. First, people gave too little, then they began to use such large doses that many children developed toxic reactions. One has to remember that the kidneys are the site at which sulfathiazole and sulfadiazine can produce their immediate and early toxic effects. It is especially true of children that when they have a severe infection, they may be quite dehydrated. It is dangerous to push

too large doses into dehydrated children, being sure that adequate fluid is administered to maintain a good flow of urine.

The dosage in general, if one goes by thumb, is approximately 1 gr per pound first twenty-four hours in any serious infection. If a child is seriously ill, one-half to three-fourths of this amount is given as an initial dose. In pneumonia, the initial dose is $\frac{3}{4}$ gr per pound, and then 1 gr per day per pound divided into four or six doses, whichever is most convenient. A day or two after the child's temperature has returned to normal, this can be cut down to one-half gr per day per pound, and kept up a few days until the infection is obviously well under control.

Sodium sulfadiazine can be given in 5% solution by clysis under the skin, and it can be used in such concentrated solution administered by syringe quite readily. In infection, where vomiting is present, this is satisfactory. These drugs cannot be given rectally by rectum. With sodium sulfadiazine, the concentration as high as 10% can be used under the skin.

DISCUSSION

DR KEEFER: Dr DAVIES spoke about the treatment of acute laryngotracheal bronchitis. He told us the disease that frequently starts abruptly, is seen frequently in children under the age of two years, associated with a variety of organisms, including streptococcus, staphylococcus and pneumococcus. He also told us that one should not use morphine in the treatment of these patients. He emphasized the importance of a humidified room with a temperature of 70 to 75°F. He was not in favor of cold or hot treatment; he advises the use of the sulfonamide oxygen and, in some cases, tracheotomy.

The first question that has been submitted answered in large part by Dr DAVIES in his paper is as follows: Discuss the treatment of acute laryngotracheal bronchitis, with reference to the effect of croup tents and steam inhalations, to the use of cold, outdoor air and to the use of the sulfonamides. The criteria for tracheotomy and for intubation should like to have him define more clearly and for tracheotomy.

DR DAVIES: That is not an easy question to answer, since I am not a laryngologist. However, intubation is still favored by some in this country, the trend is definitely toward tracheotomy. The measure of this sort must be undertaken. The otologists tell me that the trend is also toward medication and away from surgical treatment. The child is put at rest in a humidified room, still is administered and in general, supportive measures. When that is well done, it is possible to avoid the number of children who require tracheotomy.

One difficulty with intubation is that the tubes cannot be inserted without considerable tracheal

the swollen tissues. As the child breathes and coughs, there is constant motion of the tube, which tends to cause necrosis and ulceration of the mucous membrane, with subsequent scar formation. Occasionally an operation is required to remove the tube.

Indications for tracheotomy itself are not always easy to define. Certain things must be borne in mind. One should not be guided by the child's voice. Some children have unaffected voices, and yet they may be in severe distress. One should be guided most of all by the general condition of the patient. How restless is the child? How cyanotic or fatigued is he? If the disease progresses and the child becomes weaker and weaker, a point may be reached where the child actually seems to relax. To the untutored eye, the patient may seem better. However, this change is a great pitfall, because actually it may be the stage before the end. Therefore, it requires some experience and considerable judgment to decide when tracheotomy should be done. In general, it should not be postponed until the child is completely exhausted, because death may occur quickly.

Tracheotomy, of course, is not without hazards. When it is done, the child usually gets considerable relief. It also enables one to insert a catheter and remove some of the secretions in the upper bronchi. I might add that now and then the bronchoscope is useful in removing thick crusts and secretions that plug the bronchi. In the presence of atelectasis, bronchoscopy may be advisable to relieve the obstruction.

DR. KEEFER: The next question is for Dr. Finland: "What is your opinion concerning the use of convalescent serum in the treatment of virus pneumonia?"

DR. FINLAND: That is a difficult question, and there is very little experience on which to base the answer. I might say first of all that there is no precedent to indicate that one might expect a good result from the use of convalescent serum, even if it is assumed that a virus is the etiologic agent. To my knowledge, there has not yet been demonstrated, either experimentally or clinically, any disease in which a cure has been accomplished by the use of the immune serum in a virus infection *after the infection has become established*.

I am certain that if there is anyone here who has seen a patient recover after receiving such convalescent serum, especially in large amounts, he would assume that the recovery was related to serum administration, and I suppose that in a single case that might be true. There is, of course, the possibility of modifying the disease, such as is supposed to occur in measles, and this cannot be excluded in virus pneumonia. However, I think one thing should be said: if convalescent serum is given, general experience with other infections indicates that fairly large amounts should be used. It would be interesting to find out whether such infections do respond. I hope that this will be tried under well-controlled conditions, and that it will yield some useful results.

DR. KEEFER: The next question is for Dr. Janeway: "How common are serious blood and kidney reactions with small doses of sulfadiazine, small doses being defined as ½ gr. per pound or less given for less than four days?"

DR. JANEWAY: I have answered this question indirectly before. I do not believe that anyone ought to begin treating a patient with an infection, except one in the urinary

tract, with a dose of that size. Therefore, this should not happen. However, one may say that serious kidney reactions would probably be rare with a dose of less than ½ gr. per pound per day.

Serious blood reactions, as I pointed out before, practically only occur after a period of ten days of chemotherapy. The size of the dose doubtless has some influence on whether a patient develops agranulocytosis. This is certainly commoner with large doses than with small ones. But I do not believe that the dose is the whole factor, by any means. I might toss the ball to Dr. Finland, who is much more experienced than I am. Do you think agranulocytosis is much less apt to occur with small doses, provided they are carried over a long period of time?

DR. FINLAND: I do not know whether it is more or less frequent, but it certainly does occur with small doses.

DR. KEEFER: I am going to give the next question to Dr. Davies: "Should sulfadiazine be given to every case of acute otitis media?"

DR. DAVIES: That is a hard question to answer. The practitioner who first sees the patient in the home has the most difficult choice and decision to make. In the first place, one is not always treating just the acute otitis. Furthermore, the age of the patient makes a great deal of difference. Very often the past history enters into the picture. If a child has been subject to repeated infections of the upper respiratory tract,—sinuses and so on,—one should be more ready to use the sulfonamides in the early stages of acute otitis media than in a child who, up to that time, has been in robust health.

I am sure that the general appearance of the nose and throat makes a difference. A child with large, bulky adenoids, a postnasal purulent discharge and possibly with swollen tonsils may require the early use of the sulfonamides.

Then there is the appearance of the ear itself. We are all familiar with the child who has had a mild cold and awakens at night with earache. What steps should be taken beyond the use of nose drops? If, in addition to the other considerations, the ear itself is acutely inflamed and bulges markedly, even though one may be dealing with a simple catarrhal condition, I am in favor of opening the ear and using sulfathiazole or sulfadiazine, taking a culture at the time the ear is opened.

The number of cases of mastoiditis seen nowadays is much less than formerly, and it is difficult to escape the conclusion that in some measure the reduced incidence is due to the wider use, in selected cases, of sulfonamides.

DR. KEEFER: The next question goes to Dr. Finland: "Will you discuss briefly the parenteral use of sulfonamides, the indications, the route of administration, the concentration and the question whether or not alkalies should be given along with sulfonamide treatment?"

DR. FINLAND: This subject has been covered by Dr. Janeway, but there are a few points worth emphasizing. The most important point I should like to drive home is that, whereas in general one should faithfully follow the instructions that come with the packages in which drugs are contained, because the instructions are usually approved by the Food and Drug Administration and also by the Council on Pharmacy and Chemistry of the Amer-

ican Medical Association, this is one exception. The Food and Drug Administration does not permit anyone to include in the literature directions for the use of sulfonamide drugs by the parenteral method, except as a sodium salt, given as a 5 per cent solution in distilled water. We used it once or twice that way, but we certainly have not adopted this method as a routine. We almost always give it in physiologic saline solution, chiefly because it is more convenient.

Several points concerning parenteral therapy should be emphasized. It should never be given in the same apparatus or together with blood, because clots may form when the sodium salts are mixed with whole or citrated blood. If one uses glucose solution, one should never permit it to boil in the presence of the drug, because the glucose inactivates the drug by combining with it to form a compound that is inactive when given parenterally. If given in distilled water, intravenously, it should be given only in a 5 per cent solution. In infants or in adults where it is not possible, not feasible or not convenient to use the intravenous route, or when intravenous injections are undesirable, the subcutaneous and intramuscular routes may be used.

British and Canadian physicians resort to the intramuscular use of high concentrations of the drug. There is one has to use distilled water because the drug is not so soluble in saline as in distilled water. Most of the sodium salts are not soluble in saline in more than 2 or 3 per cent concentration, at least, they do not stay in the solution very long. The British originally used sodium sulfapyridine in a 33½ per cent solution intramuscularly and noted few complications, although sloughs did occur, particularly when some of the material escaped in the subcutaneous tissues. Fewer complications have been noted with the sodium salts of other drugs than with that of sulfapyridine, but in general the intramuscular use of the high concentrations is not desirable, because of the possibility that high concentrations will get into the subcutaneous tissue and produce irritation. Since the sulfonamides are usually given parenterally to the sickest patients, who have frequently lost a good deal of fluid by sweating and vomiting, and who have had difficulty in taking adequate amounts of fluid by mouth, we like to use the drug in smaller concentrations—namely, in 0.5 or 1.0 per cent concentrations in saline solution. This makes it easy to administer and also makes it necessary to use a fairly large volume of fluid.

The indications for the use of any parenteral sulfonamide drug are the same as those for the drug itself, except that the patient finds it difficult or impossible to take it by mouth, particularly if he is vomiting a good deal, or in extremely ill patients where a few hours are important. In general, it is advisable to stop the parenteral use of the drug as soon as it is possible to give it by mouth. With the high concentrations that are attained soon after injection, the drug is brought rapidly to the kidney, where renal complications are much more likely to occur in the continuous parenteral therapy than when oral therapy is used.

The dosage of drug used parenterally is essentially the same as that given orally. The initial dose is identical. If sulfathiazole is used, it is preferable to divide the subsequence daily dose, if it is necessary to continue it parenterally, into three equal parts, and to give them every eight hours. If sulfadiazine is used it is possible to give half the daily dose at twelve hour intervals.

Concerning the use of alkalis, the incidence of untoward renal and urinary tract complications is somewhat less if the urine is maintained on the alkaline side. It is possible to maintain higher concentrations of the drug in the urine without precipitation in an alkaline urine, as compared with an acid urine, and if renal complications occur,—hematuria and so forth,—the administration of alkalis such as sodium bicarbonate by mouth or sodium lactate intravenously, is advisable. These alkalis are given to the point where an alkaline urine is obtained and maintained. Whether they should be used routinely is a question that depends a good deal on whether one may or may not give alkalis in large amount to the patient whom one is treating. They are not necessary in most cases with the usual dosage of sulfadiazine, provided the fluid intake and output are adequate.

DR KEEFFER: I gather, then, that in giving the sulfonamides parenterally, the sodium salt in 5 per cent solution in distilled water, given intravenously, is *not* the method of choice. If it is dissolved in physiologic saline solution, 0.5 to 1% is high as 3 per cent may be given.

The next question goes to Dr Janeway: 'What is the difference between the use of sulfonamides in children and in adults?'

DR JANEWAY: I do not think that the fundamental principles are the least bit different. The differences lie in the way children and adults react to disease. Children vomit more readily than adults do. Therefore, one has to resort to parenteral therapy more frequently with them than with adults. Children unfortunately void more or less at will, and not in response to the dictates of convention, therefore it is difficult to keep track of the fluid output. Anyone treating a child intensively has to be more alert in looking for renal complications. With an adult, all one has to do is to have the nurse collect the urine in twelve hour lots. This can be done in the home by using a quart milk bottle, and it is easy to see whether the output rises or falls. But with children it is not so simple. One has to depend more on the answers of the mother or the nurse, and more particularly on the examination of the urine, looking for red cells. The third thing, which I pointed out before, is that the white-cell count is a fickle guide whether or not one should use intensive treatment in children, because there are so many abnormal responses of children's blood to infections. However, I believe that, taken all in all, the differences between chemotherapy in children and in adults are not great.

DR KEEFFER: Here are two questions for Dr Davies: 'What are the indications for the use of nose drops?' 'What type of base should be used, oil or water?'

DR DAVIES: The latter question is easy to answer—water. But the indications for the use of nose drops are not quite so simple. I am quite sure that we use them too much. One might say that with a simple rhinitis nose drops are scarcely necessary. However, if the infant is having trouble in breathing at feeding time, some use of shrinking nose drops before feeding is worth while. If there is definite nasal obstruction, especially if there is a purulent discharge and evidence of sinusitis and otitis nose drops should be used.

It is hard to choose the types of nose drops, nowadays because there are so many. We start with ephedrine, 1

per cent in saline solution, sometimes increasing it to 3 per cent. There are various proprietary preparations on the market, some of which now incorporate sulfathiazole or sulfadiazine. But I shall pass the question of the addition of sulfonamides to nose drops over to Dr. Janeway. Personally, I believe that the sulfonamides are not necessary in nose drops, but I am open minded about it; possibly Dr. Janeway will have more definite opinions on the subject.

DR. JANEWAY: I am not open minded about it. I do not think that sulfonamides ever should be used that way. Drugs are coming in that may be effective in these solutions, such as penicillin. I can see no reason for putting the sulfonamides in nose drops, for the simple reason that they do not remain long enough to do any good.

When one is not open minded, one is apt to be wrong. However, I believe that the indiscriminate use of these drugs in nose drops is wrong. It is easy to sensitize people through the nasal mucosa and the skin, and the use of sulfathiazole in nose drops is just as bad as some other uses, such as in ointments for skin infections. The latter should not be used as a routine. In the first place, one can clear up impetigo with agents that are more definitely bactericidal than sulfathiazole ointment, which has to be put on every three hours to do any good. I have seen a number of cases in which sensitivity to the sulfonamides originated from the local use of relatively small amounts of the drug; the patients reacted when given the drug by mouth for more serious infections later on. That is particularly true of sulfathiazole, which is an excellent sensitizing agent, so far as we can find out. The incidence of sensitivity is high.

Since sulfathiazole will be used more in the coming year or two, it is rather important not to employ it in cases in which its value is questionable.

DR. KEEFER: Dr. Finland, will you say something about the problem of sensitization?

DR. FINLAND: This is a rather difficult subject. Certainly some men who are concentrating their efforts on the treatment of allergic children look with awe on those who hand out sulfonamides on the least provocation and even on those who use sulfonamides for all infections. They are afraid that these patients will die some day from a subsequent dose of a sulfonamide drug. At least, so it was said at a meeting of the Academy of Pediatrics.

There is no doubt that sensitization to sulfonamide drugs has occurred. As Dr. Janeway has mentioned, the worst offender is sulfathiazole. Such sensitization can occur at any time, particularly in a patient who has had drug fever or a skin rash or in the rare cases of jaundice. It may occur after the first dose, and may give a very vigorous reaction, with a high fever and chills. I know of a patient who had a high fever with jaundice, and almost a fatal reaction after a single dose of sulfathiazole given a few days after a similar toxic reaction that followed a course of sulfathiazole therapy.

How often sensitization occurs, how long it persists and whether it decreases with time or stays the same are questions that are difficult to answer at present, because the data available are extremely inadequate.

One thing is certain: in general, sensitization to any one drug, in the sense I have mentioned, does not mean necessarily sensitization to all other sulfonamides, and usually it is possible to administer a different drug at another time. If necessary because of the nature of the

infection, it is even possible immediately after the discontinuance of one sulfonamide drug to start giving another. Exceptions to this are probably extremely rare.

Sensitization is usually manifested by the occurrence of a fever or a rash, or both, but is sometimes manifested by other phenomena, such as the appearance of jaundice and enlargement of the liver, and in some cases by other reactions, such as those involving the central nervous system, which I have been fortunate enough not to encounter.

DR. KEEFER: General practitioners and pediatricians are using the sulfonamide drugs for almost every infection. They maintain that many children are being saved from otitis and its resultant mastoiditis, bronchitis, pneumonia and, when sulfadiazine is used, possibly meningitis. Some pediatricians are practical minded enough to give these drugs in proportion to the symptoms, and not in proportion to the body weight. Under these circumstances, illnesses are cut short, so that the drugs are used for only two or three days. Dr. Janeway, will you give one and, if possible, two sane reasons why this practice should not be followed in all early cases of respiratory disease?

DR. JANEWAY: This is a difficult question to answer. Many are saying that they give sulfonamides according to the extent of the respiratory infection, and they claim that the illness is short lived and does not lead to complications.

The only thing one can say is that the vast majority of respiratory infections are relatively mild diseases that subside without doing the patient any great harm, and it is questionable whether one should simply administer drugs on a perfectly blanket routine for any sort of infection. One might as well say that any time a person's heart goes faster than 100, one would give digitalis, and I think the reasoning would be much the same.

It is true that the majority of complications of the virus infections that cause the usual epidemic respiratory infections are bacterial in nature, and it is quite likely that a certain number of these can be prevented and diminished in severity by the administration of the drugs. However, against routine is the problem of sensitization, and the extent of that problem we do not fully know as yet. Also toxic reactions do occur. I have no doubt but that in a number of cases respiratory infections may last somewhat longer if chemotherapy is not given. But I prefer, in general, to use the sulfonamides for the treatment of infections rather than for their prevention. The administration of the sulfonamides does not do anything to the cold itself, provided it is a virus cold. In a certain number of colds due to bacterial agents it may be effective.

Concerning why the sulfonamides should be given according to the body weight rather than in proportion to the symptoms, the only answer is that we know definitely from a great body of laboratory evidence that one has to achieve a certain concentration of the sulfonamides in order to control bacterial infection. There is no doubt that a severe infection requires more sulfonamide for its control than does a very mild one. This is because in the mild infection the patient himself is controlling it to a very large extent, and all one does is add a slight deterrent to the bacteria, which enables the patient to overcome the infection. A severe infection is almost always due to a breakdown in the patient's resistance,

and the sulfonamides become the only agents that are really capable of controlling the infection until the patient rallies enough to get hold of it himself. So, to that extent, there is a rationale there.

On the other hand, one cannot cut down the dosage more than to a certain point and expect to get any results, unless one is using the drugs prophylactically. The only studies on this subject are those in the prevention of rheumatic fever. There, it becomes clear that relatively small doses, equivalent to 1 to 2 gm (15 to 30 gr.) of sulfanilamide or sulfadiazine per day, are effective in the prevention of acute hemolytic streptococcus infection

and because of that, they are effective in preventing occurrences of rheumatic fever.

On the same reasoning, one might say, Give every patient with a cold these small doses of the sulfonamides. But my own belief is that one does not have to give the drug. Three quarters or more of the colds are taken care of in the usual course of events.

DR KEEFFER I agree entirely with Dr Janeway. I do not believe that the sulfonamides should be given to every patient with a respiratory infection. I do believe that they should be given in accordance with the body weight rather than in accordance with the symptoms.

THE LATERAL VIEW IN THE ROENTGENOLOGIC DIAGNOSIS OF LESIONS OF THE COLON*

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BOSTON

IT IS a well known fact that roentgenologic diagnosis of diseases of the colon, especially those of the sigmoid and rectum, is one of the more difficult branches of roentgenology. The lower colon has repeatedly been called the 'dark spot' of the gastrointestinal tract, and this statement has been especially true for the sigmoid and the lower descending colon, the rectum being easily accessible by other means of examination such as the proctoscope and, last but not least, the surgeon's examining finger.

It is, however, surprising as well as depressing to note how many lesions in these areas have been overlooked in the past, and how many are still missed in spite of numerous efforts to approach these regions in a more thorough and methodical manner. These efforts are highly important, since lesions of the lower colon are in the majority of cases malignant or premalignant.

Failure of the roentgenologist to detect early lesions has given rise to a pessimistic attitude on the part of the surgeon that is reflected only too well in the surgical literature. There we find comments such as the following, made by Bowman¹ as late as 1938: "A negative barium enema should not be regarded as diagnostic, since a majority of the tumors of the rectum do not show a filling defect. As a matter of fact, the majority of these lesions do show a filling defect, and the question here apparently is, What are the reasons for the failure of the roentgenologist to demonstrate these defects?"

The answer appears to be twofold—the peculiar anatomic conditions of the structures of the lower

gastrointestinal tract, and the failure to employ some or all of the helpful procedures that have been devised for the examination of these areas. Let us consider these two points.

Figure 1 reveals why a small tumor situated on the posterior wall of the colon (B) is so easily

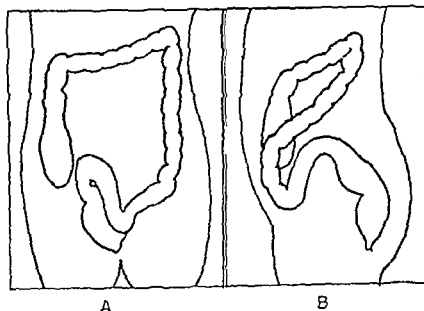


FIGURE 1 Schematic Drawing Showing the Usual Relations of the Pelvic Segments of the Colon

A shows how a tumor in the upper rectal ampulla or in the sigmoid can be completely hidden in a posteroanterior view by overlying unaffected structures. In B a lateral view the rectum and sigmoid are shown in their entirety with no overlapping of the loops.

overlooked in the anteroposterior view (A). The tumor is entirely hidden behind the barium shadow of either the completely filled loop of colon or, worse, of two overlapping loops or, still worse, of both. Since the rectum is a wide, hollow tube with the sigmoid arising from it at an oblique angle, there is overlapping of loops of colon in a majority of cases. Knowledge of these anatomic difficulties has led to the development of several

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helpful procedures for the examination of the lower colon and, as a matter of fact, of the entire gastrointestinal tract. It is the purpose of this

cated the use of air in the examination of the digestive tract, and in 1923, Fischer³ published his method of double-contrast enemas, which is still in



FIGURE 2. *Annular Filling Defect of the Sigmoid (Case 1—adenocarcinoma).*

Note that the defect is well shown in the lateral view but is invisible in the posteroanterior projection.

paper to remind the roentgenologist as well as the surgeon of these procedures, for which no priority

common use, or at least should be. Further studies include the oblique and the lateral view, both



FIGURE 3. *Large Filling Defect of the Sigmoid (Case 2—inoperable adenocarcinoma).*

Note that the defect is not visible in the posteroanterior view but well outlined in the lateral projection.

is claimed but which unfortunately are not so widely or so routinely in use as they should be.

One of these methods is the double-contrast enema. As early as 1910, Cole and Einhorn² advo-

rutinely used in our x-ray department. The latter has proved particularly helpful in a large number of cases. All these procedures have been published and their importance emphasized, notably

in the more recent papers by Wolf,⁴ Stewart and Illick⁵ and Robins and Altman.⁶

We shall present the routine x-ray technic successfully employed in our department, typical case histories and accompanying illustrations.

A word should be said concerning the preparation of the patient. This is as essential a part of

After the enema is expelled, the patient is again fluoroscoped. If evacuation has been thorough, the remaining barium coats the colonic mucosa. If too much barium remains, fluoroscopy is repeated after further expulsion. A posteroanterior and a lateral film are then taken. In a majority of cases, it is possible in this way to gain a valu-



FIGURE 4. Filling Defect of the Proximal Transverse Colon (Case 3—carcinoma).

Note the improved visualization in the lateral view, in which the extent and character of the lesion are clearly shown.

the examination as are radiography and fluoroscopy. Without proper preparation, which essentially means cleansing, no adequate examination of the gastrointestinal tract is possible. For the colon, we use the following procedure: On the day prior to examination, 60 cc. of castor oil is given. One should insist on this medication unless a definite clinical contraindication exists. On the evening prior to examination, a high cleansing enema is given. The enema is repeated on the morning of the day of examination. The patient is then brought to the fluoroscopy room and put on the fluoroscopy table in the supine position. The enema is allowed to flow slowly into the rectum, and the patient is repeatedly rotated to the right- and left-oblique positions while being fluoroscoped. Of special value is the right anterior oblique position, which yields a better visualization of the rectosigmoid junction. A spot-film device allows one to take quickly small films of any suspicious area in the position best suited for its demonstration as determined by fluoroscopic examination. The entire colon is then filled to the cecum in the same manner, and a posteroanterior and a straight lateral film are taken immediately on the Bucky table.

able impression of the condition of the mucosa of the colon. If doubt concerning the diagnosis still remains, a double-contrast enema is employed. The colon is slightly inflated by air and films or spot films are taken. It should again be emphasized that all these examinations are done, and without exception should be done, under fluoroscopic control.

Whereas this procedure is not only time consuming but a little more expensive than others, at least four 14-by-17-inch films being taken, its value cannot be overemphasized.

The following 3 cases and accompanying radiographs are typical of the large number we have examined.

CASE REPORTS

CASE 1. The patient, a 60 year old man, had had loose stools all his life, recently with some gas and slight weakness but without weight loss. He had never had bloody or tarry stools. On physical examination, he appeared to be fairly well nourished. The head, heart and lungs were negative. The abdomen was slightly tender but no masses could be palpated. On rectal examination, nothing was found with the exception of a slightly enlarged prostate. A barium enema showed a constant annular filling defect in the sigmoid 18 cm. above the anal opening (Fig. 2). A colostomy was done,

and was later followed by a combined abdominoperineal proctectomy, with resection of the sigmoid. The pathological report was adenocarcinoma, Grade 2-3.

CASE 2. The patient, a 59-year-old woman, complained of increasing diarrhea,—instead of former mild constipation,—with no abdominal pain but with occasional small flecks of blood in the stools. She had been operated on for a pelvic abscess 1 year previously and had since lost 6 pounds. On physical examination, the head, chest and abdomen were essentially negative and no masses could be palpated. A barium enema revealed an organic filling defect of the sigmoid (Fig. 3), which proved to be an inoperable adenocarcinoma with extensive local and distant metastases.

CASE 3. The patient, a 45-year-old woman, had been well until 1½ years previously, at which time she had her first attack of diarrhea. These attacks had since occurred more frequently. She had nausea, indigestion, gas, a weight loss of 35 pounds and pain in the right upper quadrant of the abdomen, radiating to the back. On physical examination, the head and chest were essentially negative. An irregular abdominal mass could be palpated in the right upper quadrant. Roentgenologic examination showed a large organic filling defect in the proximal transverse colon (Fig. 4), which at operation proved to be a carcinoma. No liver metastases or adhesions were found. A transverse ileocolostomy was done.

Cases 1 and 2 are typical of many in our series. The extent and type of lesion are well shown in the lateral view in both cases. They could not have been diagnosed or even suspected from the

routine posteroanterior view, for the sigmoid in the affected area ran in a sagittal plane.

Case 3 differed from Cases 1 and 2 in two respects: the lesion was in the transverse colon, and it was visible also in the anteroposterior projection. However, comparison between the two views reveals the markedly increased diagnostic possibilities of the lateral projection. The exact extent of the tumor, the area of annular constriction and the shelving at the borders of the tumor are clearly demonstrated. The posteroanterior view, on the other hand, shows only indefinite disease.

SUMMARY

The advantages of the lateral view in the examination of the colon, with special reference to the sigmoid, are described, and an outline of the technic is given.

Three typical cases are described and illustrated.

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MEDICAL PROGRESS

ORTHOPEDIC SURGERY (Concluded)

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Clostridia Producing Gas Gangrene

CLOSTRIDIA (spore-forming anaerobic gram-positive bacilli) are normally saprophytic. A number of them under suitable conditions may become pathogenic and produce gas gangrene, and one of them is the cause of tetanus, which is discussed in the following section.

Gas gangrene is a mixed infection, but certain of the clostridia are usually essential etiologic factors. Anaerobic putrefactive nonhemolytic streptococci may, however, produce an infection at present indistinguishable from gas gangrene.

Clostridium welchii (*Bacillus perfringens*), *Cl. septicum* (*B. oedematis maligni* or *Vibrio septicum*), *Cl. oedematiens* (Novy) and *Cl. oedematoides* (Sordelli) are each capable of producing serious gas infection. One usually predominates in association with one of the others and also with one or several of the following less important clostridial pathogens that may augment the infection: *Cl. histolyticum*, *Cl. fallax*, *Cl. sporogenes*, *Cl. lentoputrescens* (*putrificum*) and *Cl. bifermentans*. These latter, while contributory to the infection, do not alone seemingly possess sufficient aggressiveness to cause clinical gas gangrene and toxemia. These clostridia may be found in gas infection in association with many other bacterial species, both aerobic and anaerobic, including hemolytic streptococci.

Identification. Because fatal gas bacillus infection may become established with great rapidity, early etiologic identification is of the utmost importance. This cannot await cultural studies but must depend on local signs, although toxic manifestations may be strikingly significant. The mere presence of considerable numbers of large gram-positive bacilli in smears of wound exudate does not establish a causal relation. Local signs include the following: gas, evidenced by fine crepitus on gentle palpation about the wound, by bubbles expressed from the wound through the exudate, or by x-ray study; odor—putrefactive and mouse-like smells, the latter being seldom present but when found being diagnostic of infective gangrene

of muscle (Qvist²¹) and at once stamping the infection as serious; and local pain and edema, which may be conspicuous. *Cl. oedematiens* when predominant may produce a lesion characterized by rapidly progressive massive edema with little or no gas or odor but with profound toxemia. In gas infection, toxic manifestations vary with virulence and toxigenicity and are therefore not dependable under all circumstances. There is an abrupt rise in pulse—the first sign of onset. This is especially noteworthy if accompanied by a rise of blood pressure. The temperature may be high (up to 105°F) in patients with good resistance, but slightly elevated in mild infections; if subnormal, with rapid, thin pulse and other signs of shock or hemorrhage, it is a bad prognostic sign.

Identification by cultural methods should be made immediately for subsequent specific antitoxic therapy, but this should not delay operative intervention or the immediate administration of polyvalent antitoxic serums.

Toxic factors. A number of toxins can be demonstrated, and considerable study has been made of their action in animals. Toxic effects in man, although they may be profound, have not been clearly defined (Wright⁷). Each of the group produces a specific antitoxin.

Source. Pathogenic clostridia are normal inhabitants of the intestinal tract of man and domesticated animals. They persist for long periods as spores in soil, especially where manure has been used as fertilizer, and in street dirt. However, analyses of the flora of fresh wounds, inflicted under widely diverse circumstances, commonly reveal the presence of clostridia capable of producing gas infection, often in considerable numbers. There is therefore ample justification for assuming the presence of pathogenic clostridia in such wounds regardless of the circumstances attending their infliction.

Pattern of infection. Gas bacilli are normally anaerobic saprophytes. They do not become pathogenic unless certain conditions peculiar to their needs exist in the wound. The condition fundamental for pathogenicity is a sufficiently low concentration of oxygen in the involved tissues to allow the spores to germinate, the bacilli to multiply, and toxins to be produced. This con-

*The articles in the medical progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp., Springfield, Ill., 1942, Charles C. Thomas Company, 1942, \$5.00).

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dition is apparently created as a result of impairment of the blood supply to the part either by local trauma, by vascular shock or injury or by vascular degenerative changes or by a combination of these.

Clostridial gas infections vary widely from innocuous and self-limiting to fulminating and hopeless. Other factors being equal, the severity of the infection is dependent on the tissue involved: those infections that are confined to cellular connective tissues are mild, and those established in devitalized muscle are apt to be grave and give gas gangrene its evil name. This distinction, recently re-emphasized by Qvist,²¹ must be clearly recognized. It is of great importance, both clinically and academically. Clinical differentiation between the two types of infection is definite.

In the first place, infections of cellular connective tissue by clostridia are probably much commoner than those in devitalized muscle. The inflammatory reaction is a cellulitis in general comparable with that of other organisms and noteworthy in respect to gas formation and gangrene. The infection may remain localized in the devitalized elements and cease when these have been exhausted; or it may spread slowly along fascial planes and subcutaneous tissues. So long as muscle is not involved as a rule the infection remains relatively mild: the mousy smell of muscle involvement is absent, and toxemic manifestations are not severe—the temperature is commonly not high, although the pulse rate is often considerably elevated. Although these signs are indistinguishable from those of early muscle infection, they are not comparable with the profound toxemia of a well-established infectious gangrene of muscle. This mild form of infection, often self-limiting and commoner in civilian than in military practice, may well explain the cures claimed for x-ray therapy in gas infections.

In the second place, when muscle is infected by gas bacilli, sepsis spreads rapidly and toxemia is profound. Under favoring conditions clostridial saprophytes present in the wound develop a striking virulence, which is quickly enhanced—within a few hours—by toxigenicity and invasiveness. Bacteria swarm through the injured portion of the muscle, destroying it. Next, the muscle distal to the wound, having a diminished blood supply but being still somewhat viable, is invaded. Extension occurs along the interspaces between fibers, which become choked with exudate and bacteria. The exudate is free of leukocytes unless the infection is complicated by pyogenic cocci. Disintegration of sarcolemma ensues, and the muscle fibers are then entered and disintegrated

by the bacteria. Fascial planes afford favorite avenues of extension. Invasion is considerably facilitated by thrombosis, which cuts off the blood supply, thus offering a new field for bacterial spread. Metastatic infection to distant muscle groups is sometimes seen. It occurs through septic embolism, but as a rule the clostridia cannot survive in the blood stream. Invasion proximal to the wound is not held in check for long. Uninjured muscle with an intact blood supply may provide a barrier for only a short time, often not long enough for the surgeon to intervene before it is too late. The infection may involve a single muscle—more commonly a muscle group—or a segment of a limb. The skin at the wound margin passes slowly and progressively through phases of redness, bronzing, duskiness and finally the blue and black of necrosis. The extent of skin gangrene is always far short of that of muscle necrosis. Gas formation may be apparent late or not at all. It is usually present to some degree, being revealed by gentle palpation as a fine crepitus, by x-ray examination or by bubbles expressible from the wound through the exudate. Gas formation may be profuse, at which time the margin of the crepitant area may show appreciable advance at 30-minute intervals and extend far beyond the infected region into healthy tissue. A mousy odor, often present, is diagnostic of gas infection of muscle. Rapidly spreading edema, more or less marked, is almost always one of the characteristics of the local sepsis. Clinical toxic manifestations include malaise, restlessness, apprehension and, later, prostration. An abrupt acceleration of pulse (to 120 or 130), accompanied by a rise in blood pressure, is very significant. The temperature may reach 105°F., but in patients with low resistance and a poor prognosis may be subnormal.

Cl. welchii and *Cl. septicum* are conspicuous producers of gas, and *Cl. oedematiens* of massive gelatinous edema. All these clostridia are profoundly toxigenic.

Uncommonly the muscle type of infection may be fulminating, with little or no demonstrable local edema, gas, odor or pain but with profound toxemia, accompanied by a cold pale dry skin, a pulse too rapid to count and a subnormal temperature. *Cl. welchii* has been shown to be responsible for this symptom complex; however, the same state may be produced by an anaerobic nonhemolytic streptococcus.

Management. Prevention of infection by a complete débridement, as discussed below, within four to six hours of wound infliction, supplemented by prophylactic serotherapy and chemotherapy,

largely solves the gas-bacillus problem. Animal experimentation supports the use of the sulfonamides in cases in which infection with *Cl. welchii* or *Cl. septicum*—but not with *Cl. oedematiens*—is a possibility. Sulfanilamide is the drug of choice at present, 6 gm. being given orally as the initial dose, followed by 1 gm. every four hours for seven days; locally the crystalline form is sprinkled evenly over the wound surfaces, 0.1 gm. per square inch—but not over 10 gm. in all. The prophylactic use of polyvalent antitoxin in injured persons not sensitive to the serum is also indicated as a supplement to early débridement. The dose should be adequate and is specified on the container of the preparations in use.

The early recognition of established gas infection may be of vital therapeutic importance. To this end, patients with wounds involving muscle damage should be frequently checked—every two or four hours—for mousy odor and abrupt rise of pulse. Time is essential in many of these infections. When the diagnosis has been made, the appropriate surgical procedure is carried out without delay. Chemotherapy is begun at once, if it has not already been instituted, and in this regard much time may be saved by intravenous administration. Sulfathiazole is the present drug of choice. Polyvalent antitoxin is administered in large and frequent doses, both intravenously and in the muscle—by some being injected into the normal muscle about the wound. An initial dosage of four to six standard therapeutic doses is followed by two to four standard doses every four to eight hours until the infection is under control. When the responsible organisms have been identified in the laboratory, the corresponding specific antitoxins are used in place of the polyvalent.

The surgical procedure to be adopted depends on the type of tissue infected and on the nature and extent of the infection. Infective gangrene of muscle demands either radical extirpation of devitalized or necrotic tissue and the removal of foreign bodies, or amputation. Infections involving only the cellular connective tissues and not the muscle may be sufficiently dealt with by removal of sutures and a wide opening of the wound—possibly with simple incisions in addition. The mere presence of gas in a wound and numerous large gram-positive bacilli in a stained smear of the exudate does not justify amputation. The sacrifice of a limb superficially infected as in gas cellulitis is unnecessary and reprehensible. On the other hand, to withhold radical extirpation of an infected muscle or group of muscles in the belief that the infection is confined to the cellular tissues, is to court disaster. In extensive, rapidly spreading

muscle gangrene involving whole segments of a limb, amputation, if possible at a remote level, must be done promptly as a life-saving measure. Table 1 differentiates these two types of infection and their treatment.

All gas-infection wounds, whether the treatment has been simple incision, débridement or amputation, are left wide open. Meleney²²⁻²⁴ advocates a

TABLE 1. Signs and Symptoms, and Treatment, of Cellulitis and of Gangrene of Muscle.

CELLULITIS		GANGRENE OF MUSCLE	
<i>Signs and symptoms</i>			
Relatively mild localized sepsis and mild toxemia		At first relatively mild and local (red, quickly becomes violent, spreading sepsis and profound toxemia)	
Odor putrefactive, but mousy smell/lacking		Mousy odor	
No involvement of muscle at operation		Definite change in appearance of muscle, which may be hemorrhagic or discolored, may not contract normally on pinching, or may bleed abnormally slowly or not at all	
<i>Treatment</i>			
Open wound widely, with incisions if necessary		Radical débridement, amputation (guillotine or, if favorable, open flap method).	
Pack loosely and open with sulfanilamide pack or zinc peroxide dressing		Same as for cellulitis	

loose packing, saturated with a creamy suspension of zinc peroxide—which must be of fresh medicinal grade—in sterile distilled water. The suspension is made just prior to use by adding the peroxide powder, sterilized in a dry sterilizer at 140°C. for four hours, to an equal volume of sterile distilled water. The wound is flooded with this suspension before the packing is placed, care being taken to reach all parts of it. The packing is covered with a thick layer of absorbent cotton soaked with distilled water, and the whole is covered with vaseline gauze to check evaporation. This dressing is changed daily. Trueta²⁵ advocates a loose sulfanilamide pack.

Immobilization of the limb is essential, and fluid balance (2000 to 4000 cc.) must be maintained.

Clostridium Tetani

Cl. tetani, a strictly anaerobic gram-positive bacillus with a terminal rounded spore, is at present recognized in nine different serologic types. These vary in their agglutination reactions, but all produce lethal exotoxins that are identical antigenically.

Toxic factors. The clinical manifestations of tetanus are due to the toxin produced by *Cl. tetani*. The disease in its typical form can be produced by the injection of the toxin alone. Two components can be demonstrated, a hemolysin (tetanolysin) and a toxin selective for nervous

tissue, especially motor cells (tetanospasmin). Local sepsis by the organism may be negligible or not even appreciable; it is noninvasive. Although a strong affinity exists between the toxin and nerve tissue, recovery is attended by no apparent nerve impairment. There probably also exists an affinity between the toxin and muscular tissue or the myoneural junctions. Antitoxin completely neutralizes free toxin, but has no effect on that already fixed by the nervous system.

Source. *Cl. tetani* is a common inhabitant of the intestinal tract of horses, cattle, sheep and fowls, and is found in soil, being especially abundant in that fertilized by manure. Human (intestinal) carriers constitute a fair proportion of the community. Spores may survive for many years in the tissues. Wound infection is prone to occur in those engaged in agricultural pursuits and in soldiers, although no group of persons entirely escapes the disease.

Pattern of infection. *Cl. tetani* is commonly saprophytic, and it is virtually impossible to infect healthy tissue with the spores. Under certain conditions, however, the organism becomes fatally pathogenic, solely by virtue of its toxin. Wound factors necessary to pathogenicity include the following: devitalized tissue, foreign bodies, especially dirt or the coexistence of infection by other organisms, and a reduced oxygen tension locally. Any wound in which any or all of these conditions exist is a potential source of tetanus. Although occurring by far the most frequently in war wounds and in those of people who work in the soil or about domesticated animals, the infection may appear in any wound, including burns, bites, powder (Fourth of July) burns, bedsores and operative wounds—more especially in the intestines and about the anus. It may be caused by non-sterile catgut used as suture material. Experience in World War I demonstrated that a wound may heal fully without the appearance of tetanus, only to develop tetanic infection following subsequent operation. In such cases the spores remain inactive because the conditions necessary for germination and growth were originally lacking, and also by reason of the prophylactic use of antitoxin. The eventual loss of the passive immunity conveyed by the latter, together with the creation of conditions favoring infection by a second operation, permits the development of the infection. For this reason reconstructive operations on wounds that may harbor the spores of this organism must be preceded by another prophylactic injection of antitoxin.

The incubation period of tetanus is usually seven to fourteen days, but the disease may appear as early as one day or after two hundred days. Under favorable conditions the organisms mul-

tiply slowly but do not become invasive and do not appear to produce an appreciable septic reaction when the infection is unmixed. They have been recovered from regional lymph nodes, but not from the blood stream. Metastatic infections do not occur. There is much evidence to substantiate the view that the toxin is absorbed by the lymphatics, through which it reaches the blood stream, and by the latter is conveyed to the central nervous system. The former belief that toxin reaches the brain and cord by way of the peripheral motor nerves is no longer regarded as tenable (Abel et al.²⁶⁻³⁰ and Firor et al.^{31, 32}).

Clinically the disease is found in two forms: local or ascending, and general or descending. In the local form, rigidity, sometimes contractions and less often spasm occur in muscles of the region of the portal of entry. These may be mild and disappear spontaneously, or may increase in intensity and extent, becoming the generalized form. In general tetanus the rigidity begins in the facial muscles and spreads slowly downward to include the musculature of the neck, trunk and extremities. Muscular rigidity progresses to spasm and then to clonic and tonic contractions, which may extend from localized groups into violent generalized convulsions. Trivial stimuli may initiate these seizures, which may become continuous, and finally death supervenes from asphyxia or exhaustion. It should be clearly recognized that at the time of the first sign of tetanus (muscular rigidity) the disease has already become established.

Management. Active immunization by toxoid to prevent tetanus bids fair to score a high mark in the present war. What few cases appear to develop following its use have a relatively low mortality. Such immunization, combined with prompt and skillful débridement of wounds and the administration of antitoxin, removes the serious menace of the disease.

Active immunization by toxoid consists in three subcutaneous injections of 1 cc. of the alum precipitate of the toxin at three-week intervals. This initial vaccination is supplemented by a stimulating dose of 1 cc. of the toxoid to those who incur wounds that might harbor the clostridium and also to those who are about to undergo secondary open or manipulative procedures and who have not within three months received toxoid.

In cases in which the patient has not received the initial vaccination and presents himself with a potentially dangerous wound, a dose of 1500 to 3000 units of antitetanus serum is injected subcutaneously to confer passive immunity. Prior to injection with serum the following sensitivity tests are carried out: Inject intracutaneously 0.1 cc. of a 1:10 solution of serum in sterile physiologic saline solution. The patient is sensitive if, after

twenty minutes, the wheal has enlarged to the size of a nickel and is surrounded by a reddened area. Next, instill in the lower conjunctival sac 1 drop of a 1:10 dilution of serum in sterile physiologic saline solution. The test is positive if, within twenty minutes, the eye is reddened and swollen. In addition to injection for passive immunity, the patient should be given the regular course of initial vaccination.

The problem of the management of established tetanus is one of protection of the patient against all stimuli possible, control of spasm by deep sedation, stopping the production of toxin by the wound, ridding the blood stream of free toxin, maintenance of general strength by adequate caloric intake and fluid balance and measures to prevent suffocation. To these ends the following measures have the stamp of approval of those²³ who have given this disease the most study. The patient is secluded in a quiet, darkened room. Sedation is worked out according to the patient's best individual response. It may consist in the administration of paraldehyde by rectum, 8 to 40 cc., repeated every four hours, of chloral hydrate by rectum or orally, 1 to 3 gm., repeated every four hours, or of Avertin by rectum, 0.03 to 0.06 gm. ($\frac{1}{2}$ to 1 gr.) per kilogram of body weight. If cessation of breathing is impending, artificial respiration is mandatory; for this the Drinker respirator is best. Asphyxia from laryngeal spasm demands tracheotomy. The administration of antitoxin is delayed only long enough to test the patient for serum sensitivity (if the test is positive, desensitization is obligatory). One hundred thousand units of the antitoxin is given on the first day, as follows: 5000 to 10,000 units by infiltration about the wound, 60,000 units intravenously, and 30,000 units intramuscularly. On each of the subsequent days 5000 units is given intravenously until the attacks abate. Intravenous administration must be very slow. If the anaphylactic reaction appears, the needle is at once withdrawn and 1-cc. doses of 1:1000 adrenalin are repeatedly injected into the muscle until the symptoms of shock have stopped. About an hour after the infiltration of antitoxin around the wound, excision of the portal of entry is carried out if feasible. If this is not possible, thorough débridement is substituted. A fluid diet of 2000 to 4000 calories, preferably by a nasal tube, and a fluid intake of at least 3000 cc. are necessary to maintain the general condition.

Preferential Anaerobic Streptococci

The bacteriologic status of this group has not been clearly defined. Culturally these organisms exhibit a strong anaerobic tendency but not strictly so; they are found in both hemolytic and nonhemolytic forms. They are highly pathogenic under

special conditions, which are somewhat indefinite. Such streptococci may be recovered in pure culture from chronic undermining ulcerations (Meleney²⁴) that develop in the subcutaneous tissue, either in a traumatic wound or in one created surgically to drain an infected lymph node or for some procedure upon the intestinal or genitourinary tract. It is believed that the organism is an aerobic streptococcus altered by residence in the intestinal tract or in a lymph node. It may also produce gangrenous infection of the skin in synergistic association with *Staph. aureus*.

Identification. This is by anaerobic culture, but the organisms from some lesions may be grown aerobically.

Pattern of infection. In chronic undermining ulcers, the infection is confined to the cellular connective tissues, fat and fascia, which it liquefies. Spread is slow but persistent, undermining but not infecting the skin over a wide area and burrowing along the deep intermuscular septums. Erosion of large vessels or amyloid changes may cause death after months or even years unless the patient finally gets the upper hand or the organism is eradicated by treatment. Toxic manifestations include prostration, wasting and daily rises in temperature to 103°F.

In bacterial synergistic gangrene of the skin, the lesion is confined to the skin and arises at the margins of operative abdominal and chest wounds created for the drainage of peritoneal, pleural or lung abscess. It develops slowly—during the first week or two following operation—as an edematous, exquisitely tender area of erythema. In a few days the central portion takes on a purplish hue, which slowly spreads as the area of erythema advances and there then develops frank gangrene in the portion where the purplish area first appeared. This results in a skin lesion that is gangrenous centrally and erythematous peripherally, with a purplish intermediate zone. On the central side the purplish band is sharply defined and crenated, whereas on the peripheral side it gradually blends into the reddened zone. The involved area is raised above the surrounding healthy skin. Liquefaction of the gangrenous area takes place centrally as the infection spreads. Anaerobic culture of the tissue in the reddened zone reveals the presence of these preferential anaerobes alone, whereas the tissues in this zone are hyperemic. In the gangrenous zone *Staph. aureus* is found in association with this streptococcus. The purplish zone is edematous and is the seat of dense cellular infiltration. The two organisms are believed to produce the lesion by synergistic action, since neither alone can reproduce the infection experimentally but do so when combined. The source

of the streptococci is believed to be the intestinal tract and the staphylococcus comes from the skin or is an air-borne contaminant (Meleney³⁶).

Management. In chronic undermining ulcers, the deeper ramifications and sinus tracts resulting from burrowing are laid open widely so as to make readily accessible every recess throughout the system of infected tissue. Otherwise treatment will not be successful. Meleney's zinc peroxide dressing has usually been successful provided the suspension has access to every part of the wound. Oral sulfonamide therapy is a valuable adjunct. Hurwitz and Prien³⁵ were able to clear up this infection with locally applied sulfonamide after failing with zinc peroxide. When the infection has been eradicated, skin grafting may be necessary to cover wide, denuded areas. Where burrowing has occurred, vigilance is required to prevent fatal hemorrhage from spontaneous rupture of a major vessel weakened by erosion. Every effort should be made to maintain optimal nutrition.

In synergistic gangrene of the skin, excision of the entire focus, including a zone of healthy skin, eliminates the infection. Zinc peroxide dressings are applied to prevent recurrence. Skin grafting is necessary later to cover the defect.

Anaerobic Nonhemolytic Streptococci

Morphologically, the anaerobic nonhemolytic streptococci are similar to other streptococci; culturally they are strictly anaerobic and produce gas and a putrid odor, but not hemolysis. There seem to exist a large number of strains. Adequate classification does not exist, from which it may be inferred that our knowledge of these organisms is less complete than that of the aerobic groups.

Source. These organisms are normal inhabitants of the mouth and upper respiratory, gastrointestinal and female genitourinary tracts, but may be present on the skin and clothing as contaminants. From any of these sources they may enter wounds by inoculation.

Pattern of infection. Normally harmless saprophytes, these organisms may uncommonly become highly virulent. The condition at least partly possible for this change in behavior is the low oxygen tension found in necrotic tissue or in that created by trauma or a diminished blood supply.

In some anaerobic streptococcus infections is found in pure culture; in others, believed to be a definite factor in the other organisms being *Staph. n-negative anaerobic (fusiform) chetes*. The infection is putrefactive. It may follow the produce a condition indistin-

guishable from gas gangrene, or the aerobic streptococcus form, with rapidly spreading cellulitis and severe toxemia and, like the latter, possibly followed by intravascular sepsis, septic embolism, infarction, bacteremia, cardiac valvulitis and metastasis, including that of the bone, or a symbiotic form found in cases of human bite and characterized by intense edema, gas formation and putrid discharge. Each of these conditions is grave, or at least serious.

Management. These infections are best dealt with by excision, amputation or débridement, depending on the region involved. The resulting wound should be treated by the zinc peroxide technic. Sulfonamide therapy may be tried. Anaerobic nonhemolytic streptococcus antiserums have not been developed. For a complete résumé and bibliography the reader is referred to Sandusky, Pulaski, Johnson and Meleney.³⁷

Bacteroides and Fusiform Bacilli

The bacteroides and fusiform bacilli comprise a large group of pathogenic, gram-negative, anaerobic bacilli that are non-spore-forming. About them relatively little is known. They are frequently found in fresh wounds together with the common pathogens (Pulaski, Meleney and Spaeth³⁸). The designations refer to shape, the bacteroides having round ends, and the fusiform bacilli pointed ends. Their role as infectious agents may be confined to an intense local necrotizing action attributed to a powerful endotoxin.

TREATMENT OF WOUNDS

The seven cardinal principles that constitute the modern treatment of wounds rest on the basis of natural resistance to bacterial infection and the innate capacity of tissue to repair. These are as follows:

- A minimal time between the infliction of the wound and the institution of definitive treatment.
- The control of shock.
- The excision of devitalized and necrotic tissue and the removal of foreign bodies.
- Drainage by exteriorization.
- Rest by immobilization.
- The maintenance of a normal nutritional state.
- Immunotherapy and chemotherapy.

Time Factor

Given similar conditions, the aftereffects of a wound are directly proportional to the time interval between infliction and the coming into active play of all the various measures directed to combating the trauma. Prompt first aid, including the control of hemorrhage, emergency splinting, morphine sedation and plasma transfusion,

is effected to combat shock at its inception. The immediate oral administration of a sulfonamide drug assures its effective concentration in the blood stream at a time when it is most needed to check bacterial invasion. By efficient stretcher and ambulance organization (automobile and airplane) the excision of devitalized tissue, removal of foreign bodies and institution of adequate drainage may be carried out within a few hours or less, when these measures are extremely valuable. The early reduction of a fracture and adequate internal and external fixation are thus made possible. Intravenous chemotherapy—if the sulfonamide has not previously been given orally—and the early administration of prophylactic clostridial antitoxin may only by such prompt action avert grave infection. Prior active immunization against tetanus now seems assured.

Shock

If shock develops, in spite of all efforts to prevent it, the condition should be treated by modern accepted methods, which are outside the scope of this paper.

Débridement

Débridement by its present-day definition specifies the early and wide exposure of the entire wound, and the excision of tissue traumatized by the forces inflicting the wound and of hemorrhagic tissue. It also specifies the removal of foreign bodies and blood clot. For full realization of the benefit of this procedure as an antiseptic measure, knowledge, judgment and skill of the highest order are often necessary. Scientific investigation and clinical experience incriminate necrotic, devitalized and hemorrhagic tissue, blood clot and foreign bodies on the ground that they are culture mediums suitable for pathogenic bacteria. Conversely, healthy tissue is highly resistant to infection. In the creation of such bacteria-favoring conditions in tissue two factors predominate: local trauma and ischemia. Ischemia is present as a result of local vascular injury or of a contemporary remote injury to a major vessel supplying the injured region. Another and constant, more or less influential element in the production of ischemia is regional vascular spasm, the result of local shock and mediated by the sympathetic nervous mechanism. This produces local anoxia and edema, which may promote further ischemia by pressure. Vascular spasm has long been recognized as a factor of considerable importance in activating anaerobic bacteria—for example, those producing gas gangrene—by the creation of anoxia. Foreign bodies, such as bits of clothing, metal and dirt, are notorious and persistent contaminators that may cause a wound to remain open, draining indefinitely, and the re-

moval of which may result in prompt healing of the wound. The extirpation of these various infectious niduses is the purpose of débridement. Obviously, the earlier this is done the better. Débridement may be classified as a prophylactic antiseptic method.

The skin should be thoroughly washed with neutral soap and water over a wide area around the wound; the region is shaved if at all hairy and the soap-and-water washing is repeated. The area is rubbed with gauze saturated with benzene to remove grease and dirt, and then with gauze saturated with 70 per cent alcohol until clean. Finally it is painted with a 1 per cent iodine and 1 per cent potassium iodide alcoholic solution, care being taken that the solution does not enter the wound (Nye³⁸).

The incision should be axial and not transverse, except that in crossing the flexor aspect of a joint of an extremity the axial elements above and below are connected by a transverse element along the joint crease. It should be ample, so as to allow free visual exploration of all wound recesses. It should be placed, if possible, so as to correspond to a standard accredited approach to the depths of the region wounded and at the same time to include the center of the wound.

The jagged and necrotic skin margins of the wound are excised for a distance of 3 to 6 mm. Skin is resistant tissue with a good blood supply and should not be ruthlessly sacrificed. In cases in which avulsion of the skin has occurred, however, Farmer³⁹ has shown that nothing short of complete excision of the avulsed portion, removal of every vestige of subcutaneous fat and reapplication of this skin as a free full-thickness graft will alone suffice to save it. This has been repeatedly confirmed.

Fat is nonresistant and has a poor blood supply, and when at all devitalized favors bacterial activity. It is a pernicious obstacle to vascularization. When under the slightest suspicion it should be widely excised. The fasciae and septums require close scrutiny for small hematomas and traumatized portions easy to miss. Cleansing with physiologic saline solution will brighten fascia, giving it a fresh appearance, and will disclose fraying, dirt and other small foreign bodies and hematomas that might otherwise be overlooked. Such tissue is especially favorable to hemolytic streptococci and should be widely excised.

Severely traumatized and hemorrhagic muscle cannot survive and is destined to provide a virtually ideal bacterial pabulum. It may be recognized by its discoloration, by loss or impairment of contractility on pinching and (the most reliable test) by diminished bleeding—that is, absent or lessened oozing—on section. All such muscle

must be excised (by scissors) well into the normal tissue.

All but grossly necrotic portions of tendon should be spared. Damaged sheaths must be excised. Divided tendons should be sutured, if possible, using fine tantalum wire.

Both vessels and nerves are resistant to infection if conditions are at all favorable. For this reason and because of their function, they should be carefully preserved. Damaged arteries should be ligated. Severed nerves should be sutured, if possible with fine stainless steel or tantalum wire or else with fine silk.

Considerable nicety of judgment is required in the removal of bone fragments in a compound comminuted fracture. Pieces of small size (5 mm. or less) devoid of periosteum or other source of blood supply should unquestionably be removed as noxious foreign bodies. Larger fragments, undoubtedly dead, may or may not be rightly removed. Such fragments apposed to normal bone and fixed to it absolutely may serve as massive grafts that are quickly replaced by living bone, and play an important favoring role in the bone-healing process. Large defects at the site of fracture are, no doubt, advantageous from the standpoint of avoiding bone infection, but they exact a terrible toll in terms of time, loss of function and nonunion. Furthermore, before removing sizable fragments the surgeon may well recall that a fractured bone is a decompressed one and need not necessarily become badly infected. On the contrary, absolute fixation by plate or screw may be expected to protect the bone from serious infection, because it is motion at the site of fracture and not internal pressure that fosters infection of bone in these cases. One may well bear in mind, too, that osteomyelitis caused by local contamination in compound fractures, at least in civilian practice, does not imply the low resistance to specific infection found in the hematogenous form. Aside from the problem of removal of fragments, bone débridement is characterized by the care exercised to conserve periosteum and blood supply.

In the methodical layer-by-layer débridement of a wound, hemostasis must be almost absolute. Fine clamps are used to minimize tissue crushing, and ligatures of cotton, silk and fine catgut are used in that order of preference. If possible, instruments are changed with each layer.

On the completion of the excision the entire wound is irrigated from within outward with large quantities of sterile saline.

The above description applies to emergency or prophylactic débridement. Therapeutic or delayed débridement is practiced according to the same principles, except that the barrier raised by the local tissue in the inflammatory fixation must

not be crossed. It thus becomes a procedure of excision of necrotic tissue that would otherwise have to be sloughed off, the removal of clot and foreign bodies and the exteriorization of undrained recesses.

It is of the first importance to culture excised tissue and exudate aerobically and anaerobically in order that accurate knowledge of the pathogenic flora may be gained from the outset. In this way subsequent management may be effectively conducted.

Drainage

Clean incised wounds, débrided early in robust patients in civilian practice, may be closed without drainage provided close follow-up and complete postoperative immobilization are possible. Such wounds may be expected to heal by first intention in a considerable proportion of cases. On the other hand, freedom from infection in extensive lacerated contused and dirty wounds and in all war wounds is not to be expected. However, early complete healing of such wounds by secondary intention should be provided for by adequate drainage. Transverse incisions of the aponeurosis are therefore made to decompress the wound and anticipate subsequent edema. The entire wound is then packed loosely with gauze saturated with boric acid ointment or vaseline to hold apart gently the walls of the wound. Such packing does not impede the clearance of discharge, irritate the tissue, or in any way promote anaerobic infection. The wound is protected against subsequent contamination by an ample dressing and the region is immobilized by appropriate external fixation.

Immobilization

The broad principle involved in immobilization is the curative effect of rest. A number of factors combine to this end. These may be divided into three groups: the control of pain, the control of absorption and the control of subsequent trauma.

Immobilization of the injured part reduces the painful afferent nerve stimuli arising out of the wound itself. These are caused by motion in the injured region, by muscle spasm and by pressure from edema. General shock is thus markedly lessened and local muscle, and sympathetic vascular spasm can subside and disappear. There results in turn subsidence of edema, with the result that there is further lessening of the pain factor.

Experimental evidence indicates that the absorption of toxic substances resulting from tissue damage, of bacterial toxins and of bacteria themselves takes place largely through the lymphatics, and it has been demonstrated that the rate of lymph flow is greatly reduced by immobilization, not only physiologically but in the presence of

edema and inflammation (Drinker and Yoffey⁴⁰ and Barnes and Trueta⁴¹). It is well known, furthermore, that toxins that are lethal in massive dose may be neutralized and eliminated without demonstrable ill effect if their rate of introduction to the blood stream is relatively slow. Clinical experience has repeatedly demonstrated the minimizing effect caused by immobilization on many toxemias.

Splinting favors wound repair by protecting new tissue capillaries from abnormal tension, twisting and bending, that is, from the repeated subsequent minor traumas caused by motion. These retard healing, lead to dense avascular scar tissue and cause mechanical spread of infection.

Nutrition

The influence of diet on wound healing has been discussed thoroughly in a previous progress report (Holmes⁴²). In general, the optimum diet for patients with infected wounds is one of high-calory, high-polyvitamin content, and this is so selected that the protein fraction is raised at the expense of the fat. Whereas the role of vitamin C deficiency in arresting the formation of intercellular substance (collagen and osseomucin) has been clearly defined, that of vitamins A and D in wound healing and in resistance to infection has not. There is in surgical infections an excessive demand for vitamins that quickly depletes the reserve supplies unless these are maintained either by diet or by direct administration. Increased attention is being paid to the part played by blood protein in tissue repair and resistance to infection and in combating the toxemia resulting from infected wounds. All the evidence points to the importance of this factor. Infection with toxemia causes a drop in the production of plasma protein, and conversely hypoproteinemia lowers resistance to infection, retards tissue repair, lowers general body tone and causes edema. The control of the protein reserve balance in the plasma and tissues in cases of wound infection has not yet been effected. Protein ingestion by mouth has so far proved to have the best effect. Repeated whole-blood and plasma transfusions have not been especially effective in raising the protein level of the blood.

Immunotherapy and Chemotherapy

The various applications of immune serums and the use of toxoid have already been discussed under management of the different infections.

The bacteriostatic property of the sulfonamides when given orally or intravenously is so clearly and widely appreciated that no further comment is required here. The local application of these drugs to fresh wounds combined with oral administration is still a somewhat controversial point,

and scientific evaluation is still lacking. One may detect a tendency away from their topical use on the clinical ground that most wounds do as well or better without as with these drugs, and on experimental grounds because of their being prone to act as foreign bodies when not dissolved, because of their toxic effect on tissue cells in high concentration, because of their inability to penetrate devitalized or necrotic tissue, and because their bacteriostatic action is inhibited by wound exudate. On the basis of physical properties—greatest solubility in serum, greatest wound diffusion, most rapid clearance from the wound and quickest excretion—sulfanilamide seems best adapted to this use. The crystals should be evenly sprinkled over the surfaces of the wound in an amount not to exceed 0.1 gm. per square inch of wound surface. For a critical review, the reader is referred to Lyons and Burbank.⁴³

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

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CASE 29301

PRESENTATION OF CASE

A fifty-five-year-old widow entered the hospital because of painless jaundice of two weeks' duration.

The patient had been in good health until three months before entry when she began to experience a feeling of pressure in the epigastrium coming on usually about two hours after lunch and lasting well into the evening. At times she felt nauseated; she very rarely vomited, and when she did the vomitus consisted of slightly sour, undigested, recently eaten food. The patient gradually developed an almost complete aversion to food and ate only small amounts of fat-free food; often she ate only toast for dinner. Four weeks prior to admission she noticed that the urine was dark brown, and the stools pale. She soon became jaundiced and the skin began to itch. The jaundice deepened, and the abnormal colored urine and stools persisted to the time of admission. During the illness her bowels remained regular, and only occasionally did she require Epsom salts for the relief of mild constipation. She had lost 10 pounds in weight during the previous three months. She believed that recently the abdomen and ankles had begun to swell.

The patient's mother died at fifty-five years of age with carcinoma of the breast. Two sisters had had hysterectomies done because of menorrhagia. Four years prior to admission the patient was sterilized by x-rays, because of persistent metrorrhagia; she had no further bleeding but continued to have a vaginal discharge and occasional pain in the right lower quadrant of the abdomen. Two years prior to admission the uterus, tubes and ovaries were removed for "fibroids."

Physical examination disclosed a thin, deeply jaundiced woman who appeared restless. The scleras were deeply jaundiced. There were many excoriations about the trunk, numerous small (1 to 2 mm.) purpuric spots about the knees and small "spider angiomas" of the arms, face, neck and thorax. The lungs and heart were normal.

The liver edge was felt three fingerbreadths below the costal margin in the epigastrium. A mass that descended to the umbilicus on inspiration was believed to be an enlarged gall bladder. No tenderness was elicited. There was slight pitting edema at the ankles.

The blood pressure was 90 systolic, 55 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a hemoglobin of 10.9 gm. per 100 cc. and a white-cell count of 9600. The urine was acid, had a specific gravity of 1.020 and showed a + test for albumin and a +++ test for bile; the sediment contained amorphous urates and 6 white cells and 6 epithelial cells per high-power field. A blood Hinton test was negative. The prothrombin time was normal. The total protein was 5.0 gm. per 100 cc., and the bilirubin 12.3 mg. direct and 17.5 mg. indirect. The stool was light brown in color and guaiac negative in four examinations. The sedimentation rate was 16, 32, 44 and 49 mm. in fifteen, thirty, forty-five and sixty minutes respectively. A gastrointestinal series demonstrated a normal stomach and esophagus. The duodenal cap was large, and the tip was narrowed, apparently by an extrinsic band or blood vessel crossing it. The second portion of the duodenum showed no constant defects or evidence of rigidity of the wall.

After two weeks of preoperative preparation, including administration of water-soluble vitamin K and glucose-saline infusions, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. AUSTIN BRUES: This appears to be a classic case of carcinoma of the head of the pancreas. I shall therefore discuss it from the point of view of seeing whether any other diagnosis will fit with the history as given.

The age of the patient is consistent with that diagnosis, the average age in most series being the late fifties. The prodromal gastrointestinal symptoms without pain and with anorexia and weight loss are common, weight loss being extremely marked in certain cases of carcinoma of the head of the pancreas. At the time the symptoms appeared the patient had progressive jaundice, which became intense, with itching. The enlarged liver and the enlarged gall bladder, according to Courvoisier's law, indicate a constantly progressive lesion low down in the biliary system. The patient had a high bilirubin, direct and indirect, an elevated sedimentation rate and a normal prothrombin time. One might expect the prothrombin time to be elevated in jaundice; however, if the lesion produced obstruction primarily, the liver might

*On leave of absence.

have been able to maintain a normal blood prothrombin level for a period of some weeks.

I should say that the chief observation not in line with this diagnosis is that of spider angiomas, which are seen characteristically in cirrhosis of the liver, and may be observed a long time before the cirrhosis becomes manifest in other ways. They also have an endocrinologic angle, since they may appear during pregnancy and may be increased, when already present in patients with hepatic cirrhosis, by the administration of estrogen. It has been suggested that spider angiomas represent loss of liver function. Since the cirrhotic liver is unable to destroy or metabolize estrogen, this vicarious endometrial manifestation occurs in the skin. It is worth remarking incidentally that this woman was sterilized first by x-rays and then by ovariectomy. In line with the theory mentioned, it might be supposed that the angiomas antedated these procedures. At any rate, they suggest, but by no means prove, that the liver may have suffered chronic low-grade damage or was cirrhotic.

Another observation not quite in line with the diagnosis is that the stools were light brown. The obstruction therefore was not complete. That may have been an erroneous judgment; such things can occur. The obstruction may not have been incomplete, although anatomic considerations make it likely that once carcinoma of the head of the pancreas gives obstruction it shortly becomes complete, and that is what usually happens, unless there are anomalous or accessory bile ducts.

The low plasma protein and ankle edema may have been due to faulty nutrition; along with spider angiomas they might suggest a long-standing, low-grade hepatic insufficiency, but there is nothing else to indicate it. The prothrombin time was normal, and I am merely going to make the suggestion that there might have been some chronic liver damage unrelated to the main lesion. The slight albuminuria is consistent with jaundice.

Among the other diagnostic possibilities worth suggesting, the first is something associated with a low-grade chronic cirrhosis that would give these manifestations. The best of these probably is hepatoma. In that case the mass thought to have been gall bladder would be the tumor. The jaundice would be due to intrahepatic obstruction, and this would account for the small amount of bile in the stool. On the whole I think that is improbable. Carcinoma of the gall bladder might be considered. In that case the mass would be the carcinoma and again the obstruction would be intrahepatic from metastases high in the biliary system. Furthermore, I cannot rule out obstruction from some uncommon cause, such as fibrosis of the pancreas, lymphoma or metastases to peripor-

tal nodes compressing the bile duct. The fact that there was no palpable spleen is against lymphoma. I am against common-duct stone: Courvoisier's law is against it, as is the absence of pain and the steadily progressive nature of the jaundice. A common-duct stone can occur in a small percentage of cases without one of these anomalous findings, but from the laws of probability it seems extremely unlikely that these three unusual features could occur together. Carcinoma of the ampulla or of the duodenum I disfavor because of the absence of blood in the stool. My final diagnosis is carcinoma of the head of the pancreas.

DR. CHESTER M. JONES: It seems to me that it is entirely probable that this woman had cirrhosis. Only a rare case with spider angiomas fails to have cirrhosis, excluding those cases observed in pregnant women. I think that this woman had severe liver damage. We do not know what the serum albumin was. The liver was certainly enlarged, and ankle edema and ascites were present. The fact that the patient had brown stools makes it conceivable that the whole clinical picture was due to intrahepatic disease alone. We have had cases of acute hepatic insufficiency with brown stools, a palpable liver, abdominal pain and fever. The important thing is that a definite diagnosis was not possible and therefore that exploration was indicated. I believe that carcinoma of the pancreas is less likely as a diagnosis than acute hepatic insufficiency or chronic liver disease with superimposed hepatoma.

DR. BENJAMIN CASTLEMAN: You are basing all your conclusions on the spider angiomas?

DR. JONES: Not entirely, but they furnish important evidence. The facts that there was color in the stool and that the patient had ascites and edema cannot be overlooked.

DR. ARTHUR W. ALLEN: I should like to add that, for some reason or other, the types of obstructive jaundice that give brown stools or intermittently brown stools are much more apt to be associated with malignant disease than with any other type of biliary obstruction. I do not know why. Frequently a little bile goes through in cases of carcinoma, particularly of the papilla.

DR. CASTLEMAN: Possibly that can be explained by the fact that the carcinoma often becomes necrotic, sloughs off and thus partially relieves the obstruction. It is seen more commonly in carcinoma of the papilla than in carcinoma of the head of the pancreas because the necrotic tumor may slough into the duodenum.

DR. GREENE FITZHUGH: This patient was operated on because her jaundice increased. We considered peritoneoscopy, but the jaundice increased

so rapidly that we thought it wiser to go ahead and do something about it.

DR. JONES: As I have said, the important thing here was to make the decision and not the diagnosis. But, in a case of this sort, one has to be prepared for liver disease as well as something outside the liver.

DR. RICHARD H. WALLACE: At operation the mass was a greatly distended gall bladder. The common duct was about 3 cm. in diameter. A mass was felt in the head of the pancreas. Fortunately we could make a diagnosis very readily because the tumor had extended through into the duodenum, or perhaps it started there, there being an area about 3 cm. in diameter with a central crater in the region of the papilla of Vater. We were able to resect the head of the pancreas with the proximal two thirds of the duodenum, and fortunately we could deliver the end of the duodenum beneath the mesenteric vessels and suture it to the end of the dilated common duct and were conveniently able to anastomose the end of the stomach to the side of the jejunum, making only two anastomoses. The patient had a smooth convalescence and is well today so far as we know.

DR. BRUES: Did you observe *typical* spider angiomas?

DR. WALLACE: She had what I consider to be spider angiomas.

DR. JONES: The pulsating sort?

DR. WALLACE: I am not sure of that.

DR. CASTLEMAN: How did the liver look?

DR. WALLACE: It was the enlarged, greenish liver that one sees with obstructive jaundice.

CLINICAL DIAGNOSIS

Carcinoma of head of pancreas.

DR. BRUES'S DIAGNOSIS

Carcinoma of head of pancreas.

ANATOMICAL DIAGNOSES

Adenocarcinoma of duodenum, involving the papilla of Vater, with extension to the pancreas and with metastases to the regional lymph nodes.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: We received a section of duodenum, 10 cm. long, with the attached head of the pancreas. On the mucosa of the duodenum surrounding the papilla of Vater was a large ulcerating tumor 3 cm. in diameter, with raised borders and a central ulceration. In the center of the crater was the opening of the common bile duct, which was markedly narrowed. The bile duct

above the constriction was dilated. This tumor proved to be an adenocarcinoma that had extended through the duodenal wall to involve the surface and a very small portion of the pancreas. There is no doubt in my mind that the tumor was primary in the duodenum rather than in the pancreas. The regional lymph nodes were enlarged and hard and were filled with metastatic carcinoma. These were close to the head of the pancreas and were probably what was believed to have been the mass within the pancreas at operation.

CASE 29302

PRESENTATION OF CASE

A forty-four-year-old single woman entered the hospital because of profuse menstrual bleeding of a year's duration.

Menarche occurred at eleven years, and prior to the present illness, periods occurred regularly, with a twenty-eight-day cycle, and lasted five days. During menstruation the flow was moderate, requiring two napkins a day. On the fourth or fifth day she often had mild abdominal cramps. Approximately one year prior to admission the patient noticed gradual increase in the amount and duration of menstrual bleeding. About four months before entry her periods began to occur every twenty-four or twenty-five days and each lasted eighteen to twenty-one days. During the first two weeks she frequently passed small and moderate-sized blood clots. During the year of illness she suffered with a "bearing down" sensation in the pelvis but there were no changes in bowel or urinary habits and no weight loss. The last menstrual period began thirteen days prior to admission and flow continued to the day of admission.

The family and past histories were noncontributory. During the week prior to admission she had had an upper respiratory infection, from which she had recovered without sequelae.

Physical examination disclosed a well-developed and well-nourished woman who seemed quite comfortable. The pharynx was slightly congested, and the tonsils slightly enlarged. There was a soft, blowing systolic murmur audible over the entire precordium, best heard in the mitral area. The lungs were normal. A firm, slightly tender, irregular mass was felt in the lower abdomen. Vaginal examination under ether disclosed a normal-appearing cervix and a small vagina. The uterus was large but freely movable, and the vaults were negative.

The blood pressure was 125 systolic, 70 diastolic. The temperature, pulse and respirations were normal.

The blood was normal. The urine was bloody. A blood Hinton test was negative.

An operation was performed on the second hospital day.

DIFFERENTIAL DIAGNOSIS

DR. JOHN ROCK: It is important throughout the history to note the terminology used in reference to the bleeding. It was profuse menstrual bleeding, which does not indicate what is commonly called "metrorrhagia." There is no suggestion of intermenstrual bleeding. The description makes me believe that this was polyhypermenorrhea and not dysfunctional flow or metrorrhagia.

"During the first two weeks she frequently passed small and moderate-sized blood clots." There was therefore some derangement of menstruation.

We are not told how large the abdominal mass was or where it was located in the abdomen, except that it was in the lower abdomen. It may have been on one side or the other, or very large or only palpable just above the symphysis. The fact that the vagina was small suggests that the vagina might have been encroached upon. The patient was unmarried; perhaps the vagina was normally small. We are told that the uterus was large, but we do not know how large—perhaps 6 or 7 cm. wide and 4 or 5 cm. thick or it might have reached up to the umbilicus. There was a mass in the abdomen, which may have been the uterus, but nothing was felt in either vault.

There was no blood dyscrasia to account for the polyhypermenorrhea. The urine was bloody, but if it was a voided specimen one would expect it to be bloody because the patient was flowing when she came in.

As I have said, we have to account for polyhypermenorrhea occurring in a forty-four-year-old woman that was associated with a mass in the lower abdomen and an enlarged uterus. Polyhypermenorrhea, that is, periods occurring at intervals shorter than the classic twenty-eight days, is not uncommon in a woman forty-four years old. Even excessive flow is not uncommon, but such marked prolongation of the periods indicates some pathology. So we might consider that it probably was due to whatever made the mass in the lower abdomen and enlarged the uterus. Following Cabot's instruction to make one diagnosis cover as many situations as possible, we had better say that the mass in the abdomen was the enlarged uterus. One can account for the bleeding perhaps by polyps, which prolong flow and result in the formation of clots. But polyps usually do not enlarge the uterus. Fibroids are of course the first thought that one would have to consider to ac-

count for all these things, probably multiple fibroids, because the mass in the lower abdomen was irregular. The patient could have had sarcoma, with or without fibroids, or she could have had endometriosis of the uterus itself. Endometriosis of the uterus is not uncommon and it does cause enlargement, which may be irregular; it usually does not cause intermenstrual flowing but increases in the amount and prolongation of the flow. It may also give enlargement of the uterus that is sufficient to be felt above the symphysis.

Then of course there is cancer. I think it is impossible to make a particular diagnosis here. Cancer in a forty-four-year-old woman sufficient to cause enlargement of the uterus and mass in the lower abdomen would have certainly given more bleeding than this patient had, and a different kind of bleeding.

We have to assume that the tumor was the uterus and that the ether examination was accurate. It is easy to mistake a tumor of either ovary for one of the uterus, and often an operation for fibroids is performed, because statistically they are the commonest cause of enlargement of the uterus, only to find that the tumor is a contiguous one of the ovary and not an outgrowth from the uterus.

Because the bleeding was of the menstrual variety we have to limit the diagnosis to fibroids or endometriosis of the uterus. How can we distinguish between these two? I do not know. Fibroids commonly give no symptoms whatever. They are troublesome only because of their size.

I think one was bound to operate on this patient with a working diagnosis of fibroids of the uterus but with the possibility of finding endometriosis or possibly sarcoma.

DR. JOE V. MEIGS: I think it is only fair to tell Dr. Rock that the patient did have a mass on one side.

DR. ROCK: If the mass on one side could be considered a tumor of the ovary then we must consider a tumor that does not interfere with ovulation. I do not know any tumor of the ovary that gives enough estrogen to increase flow without interfering with ovulation. But if the uterus is really enlarged in a woman of forty-four, we must assume some extra stimulation in the uterus, and therefore this patient might have had a granulosa-cell tumor of the ovary or, again, endometriosis of both the ovary and the uterus.

DR. MEIGS: I think the diagnoses that we made before we operated on the patient were fibroids and endometriosis. We knew there was a mass on the right side, which Dr. Rock did not know. I did not curet her because I was going to do a total removal of the uterus anyway.

At operation I found a cystic lobulated mass the size of an orange in the right ovary. One of the cysts had ruptured and there was a moderate amount of clear, free fluid in the abdomen. The whole uterus and the right ovary and tube were removed. My habit is to open the uterus before closing the abdominal wall, but this one time I did not do it. We had the patient's abdomen partially closed, when I realized I had not looked at the ovary or uterus. I stopped and opened the ovary, and much to my surprise, there were papillary areas and soft tissue inside. When I opened the uterus I found similar soft granular tissue on the endometrium, which made me think that the tumor had metastasized to the right ovary. I reopened the wound and removed the other tube and ovary.

The patient also had fibroids of the uterus and endometriosis of the pelvis.

CLINICAL DIAGNOSES

Fibroid of uterus.
Endometriosis.

DR. ROCK'S DIAGNOSIS

Uterine fibroid?
Endometriosis?

ANATOMICAL DIAGNOSES

Adenoacanthoma of uterus, with metastasis to right ovary.
Leiomyomas of uterus.
Endometriosis of uterosacral ligament.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: We received three separate specimens. First the right ovary and tube and uterus, then the other ovary and tube and finally a small piece of tissue that had been removed from the pelvic floor.

DR. MEIGS: The left uterosacral ligament.

DR. CASTLEMAN: The ovary was cystic, as Dr. Meigs has said, but the tissue inside was not really

papillary. There was a mass of soft, friable tumor, which on section proved to be exactly the same as the tumor in the fundus of the uterus, an adenoacanthoma, that is, parts of tumor were adenocarcinomatous and other parts showed squamocell change or epidermoid carcinoma. This type of tumor is quite common in the body of the uterus, and I believe has a poorer prognosis than the straight adenocarcinoma.

DR. MEIGS: I should not say that. If it is treated with radiation, the outlook is poor, but if treated with surgery the results are fairly good.

DR. CASTLEMAN: Just about the same as those in adenocarcinoma?

DR. MEIGS: Yes.

DR. CASTLEMAN: If one finds a tumor in the ovary and one in the uterus it is often difficult to tell which is primary. The fact that this tumor was an adenoacanthoma proves that it was primary in the uterus. I do not believe that we have ever seen a primary adenoacanthoma of the ovary.

DR. MEIGS: Dr. Richard H. Miller had a case of primary adenoacanthoma of the ovary here years ago; nothing was found in the endometrium.

DR. CASTLEMAN: The uterus also contained large fibroids, and the small piece of tissue removed from the uterosacral ligament showed endometriosis. So the patient had all three diseases.

DR. MEIGS: The tumor in the uterus was not localized to one area but filled the entire endometrial cavity. This made me think that the metastasis was from the endometrium to the ovary and not from the ovary to the endometrium.

DR. CASTLEMAN: Why did you not do a curettage first, Dr. Meigs?

DR. MEIGS: If I am going to remove the entire uterus, I do not believe it is necessary; furthermore, if cancer is present a curettage may still tumor. The uterus, however, must be opened before closing the abdominal incision.

DR. CASTLEMAN: I have never been convinced that a curettage will implant tumor lower down. If metastases do occur in the vagina, I believe that they get there via the lymphatics.

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AWARD TO DOCTOR JOSLIN

To have been awarded the Distinguished Service Medal and Award of the American Medical Association and thus to be placed in the group of outstanding physicians that includes Hektoen, Herrick and Chevalier Jackson is an honor of which any man may justly be proud, and we of New England may similarly be proud that the recipient is Dr. Elliott P. Joslin.

A simple man of tireless energy and boundless enthusiasm, he has devoted his life to the treatment of diabetes mellitus. He has systematically trained the patient in knowledge of the disease so that life may be prolonged and health preserved. He could

not have become such an outstanding specialist had he not had extensive general clinical experience abroad and later on the wards of the Boston City Hospital. He could never have acquired such detailed knowledge of diabetes had he not possessed infinite patience and been endowed with the ability to prevail against seemingly hopeless odds. His success would have been far less had he not recognized unconsciously that "the secret of the care of the patient is caring for the patient."

We congratulate Dr. Joslin on his achievement, and we hope that he may for many years continue the work for which so many thousands give thanks.

THE SYMBOL OF BUREAUCRACY

PHYSICIANS, with few exceptions, have been well treated so far as gasoline rationing is concerned, and their privileges have usually not been abused. They have been recognized as a hard-working, essential group of men and women, with more than average social consciousness and conscience. There has always been a tendency, in fact, to idealize their position in the community, to sentimentalize a little over their devotion to duty and their appetite for hardship and to grant them indulgence, as a class, on that account.

The fact is not to be lost sight of, however, that extra gasoline is not given as a reward for merit but as a means of enabling the physician to perform his functions in the community as efficiently as possible. He is made thereby, not a pampered idol, but a trusted public servant. The very nature of his services and the unpredictability of their character make it imperative that he should have his mode of transportation at hand. If he is permitted to have his recreation,—and the most zealous bureaucrat would hardly deny it to him,—he must have his car with him, if he is to stay on call. In all other ways he is an A-card holder, subject to the same restrictive regulations, the same lack of privilege and the same penalties that the owner of a so called "pleasure car" enjoys.

The whole question of gasoline rationing merits

a serious review for here, in the minds of many who still cherish the idea of the rights of the individual, bureaucracy has committed one of its most serious blunders. It is not that gasoline rationing is unneeded; it is undoubtedly a stern necessity, recognized as such and accepted as such by the vast majority of citizens. It is the inability of bureaucracy to distinguish between the right and the wrong ways of directing a democratic people that is disquieting. To apportion the residue of gasoline that is left over after the necessities of war and the welfare of the public have been cared for is a reasonable procedure, even if the share of each person is only a gill a month. However, to set spies among the people to determine how each shall use his microscopic share, or suffer penalty, is quite different, and one of the most amazing things that has taken place on these shores since the Stamp Act engendered in the minds of a nation the idea of freedom from oppression.

It sometimes seems as if there were fixed in the collective mind of bureaucracy not only the idea that gasoline must be saved, but that in the saving thereof the people must be scourged. One can see rising in the form of a fuel director the spirit of Cotton Mather, purging the citizens of their devils and burning the witches at the stake.

MEDICAL EPONYM

WINTRICH'S PHENOMENON

This is described by M. Anton Wintrich (1812-1882) in the section "Krankheiten der Respirationsorgane [Diseases of the Organs of Respiration]," in the first section of the fifth volume of Virchow's *Handbuch der speciellen Pathologie und Therapie* (Erlangen, 1854). A portion of the translation follows:

The change in pitch of the tympanic note over superficially situated cavities, connected via the bronchi with the trachea, larynx, mouth and so forth, by a continuous column of air, is a very pretty phenomenon. If the patient closes his mouth or swallows, thus narrowing or closing the opening of the larynx by lowering the epiglottis, the tympanic note immediately becomes fainter . . . and deeper, and vice versa [when he opens his mouth].

R. W. B.

OBITUARY

WILLIAM FESSENDEN WESSELHOEFT

1862-1943

Dr. William Fessenden Wesselhoeft died of coronary disease and arteriosclerosis on June 27, 1943, at the Massachusetts Memorial Hospitals. He was born in Boston, March 5, 1862, and graduated from Harvard College in 1884; having rowed on the freshman crew and played varsity football. After graduating from Harvard Medical School in 1887, he took postgraduate courses at the Rotunda in Dublin, and in Vienna. He was the third William Wesselhoeft in line to practice medicine in Boston.

His grandfather received his medical degree at the University of Jena in 1820. Owing to membership in the Burschenschaft League and his volunteering as field surgeon to help the Greeks in their struggle for freedom, he was forced by Prussia and Austria to take refuge in Switzerland, where, for two years, he was demonstrator of anatomy at the University of Basel. On being warned that his extradition was sought, he walked all the way to Antwerp, where he took ship for New York and settled in Siegersville, Pennsylvania, in 1824. Thus he was one of the forerunners of those many political refugees from Germany who came over in great numbers with Karl Schurz in 1848, and the many more who have followed in this past decade. Through the influence of fellow refugees, Beck and Follen, Dr. William was asked to consider a position dealing with physical education at Harvard College, but this never materialized. He became interested in homeopathy and was one of the founders of what is now the Hahnemann Medical College in Philadelphia. He moved to Boston in 1842 and, as the story goes, was refused admission to the Massachusetts Medical Society on the grounds that he failed to bleed a case of typhoid fever. His brother, Robert Wesselhoeft, likewise a physician refugee, founded the "water cure" in Brattleboro, Vermont. This was the origin of a family of physicians in New England that found in homeopathy something more to their taste than the bleeding, blistering and purging so much in vogue at that time.

William Fessenden Wesselhoeft was the son of William Palmer Wesselhoeft, a graduate of Harvard Medical School in 1857 and an ardent homeopathist of the irreconcilable, high-dilution school, with a strong personality and advanced views regarding fresh air and the value of a mixed diet. The son espoused the hygienic views of the father, but lacking any true enthusiasm for the homeopathic method he took up surgery, working his

way up through the grades to the position of surgeon at the Massachusetts Memorial Hospitals and professor of clinical surgery at Boston University School of Medicine. He introduced a new surgical knot and devised a method of sterilizing catgut that was long in use at the Massachusetts Memorial Hospitals and elsewhere.

In World War I, with the rank of lieutenant colonel and as commanding officer of Base Hospital No. 44, he took this unit to France and served with it at Pougues les Eaux. He was a member of the Boston Surgical Society and a fellow of the American College of Surgeons. He never joined the Massachusetts Medical Society, a last flicker of protest handed down from a generation that exhibited a lively hostility.

Dr. Wesselhoeft married Emily Bradley, of Boston and Brattleboro, Vermont, who died in 1931. He is survived by four daughters: Margetta, widow of the late Dr. Bigelow, formerly commissioner of health of Massachusetts and Superintendent of the Massachusetts General Hospital; Susan, wife of Mr. Renouf Russell; Alice, wife of the honorable Leverett Saltonstall, governor of Massachusetts; and Emily, wife of Colonel William A. Barron, Jr., chief-of-staff of the First Service Command. He is also survived by thirteen grandchildren, two of whom are now serving in the Marines, three in the Navy and one in the Army. There are five great grandchildren.

Besides his many relatives, Dr. Wesselhoeft leaves behind him a large number of devoted patients and a host of colleagues who, as former students and subordinates, cherish the memory of his idealism for professional honesty, his spirit of service and his sympathetic manner at the bedside.

C. W.

MISCELLANY

"THE DOCTOR'S AUTOMOBILE"

Under the above title, the following statement, signed by Dr. Emery M. Potter, president of the Providence Medical Association, appeared in the July issue of *Medical News*, the official bulletin of the association. It is such an honorable and fair appeal that further comment seems unnecessary.

In the present-day practice of medicine the doctor finds his automobile an extremely necessary and vital instrument. Consequently the publication recently of rules and regulations by the Office of Price Administration to clarify the driving permitted and prohibited under the ban on so-called "pleasure driving" has caused much comment and speculation among the profession. The question arises as to how a doctor may pursue his regular routine and at the same time have

his automobile accessible for emergencies without violating the OPA restrictions.

First let it be clearly understood that the Rhode Island OPA authorities are sympathetic with the problem which faces the doctor, and they are clearly cognizant of the fact that of all civilian groups the doctors of medicine—particularly those who are subject at all times to demands to administer to the sick, to respond to civilian disasters, to serve the Civilian Defense program, or to meet any general threat to the health of our community—have an imperative need to have their automobiles available in order to answer emergency calls promptly.

The OPA authorities here are fully aware of the shortage of doctors in the State owing to the withdrawals to meet the demands of the armed forces. Therefore they are particularly anxious to avoid the prosecution of any doctor for the violation of the rules of driving. But this desire to protect the health of the citizens and at the same time not to inconvenience the doctors of the State calls for a corresponding sincere co-operation by each physician. To date that co-operation has not been forthcoming at all times.

Several fundamental factors must be considered by the doctor as he justifies the use of his automobile for reasonable nonprofessional driving in order that he may have his car accessible for his personal use for emergency calls.

First—The doctor must realize that his professional calling places him in a preferred class, and he is obligated not to abuse the privileges accorded him. If the patient is denied the right to drive to the beach, or to drive to and from a summer home, then the doctor too must forego the same pleasures.

Second—While relaxation from strenuous work is essential for everyone, the doctor as well as the patient, the auto driving involved to reach recreational centers cannot in all fairness be more for one than for the other. Reasonable driving, even for social calls, may be undertaken by the doctor in order that he may have his automobile at hand for emergency hospital or sick calls, but the doctor must not misinterpret what constitutes reasonable driving under such circumstances.

Third—No doctor should embarrass his professional colleagues, nor should he antagonize public opinion, by flagrant violation of the OPA rules and regulations under the excuse of a physician's privilege to operate an automobile. Open violations of the restrictions certainly should merit penalty for all persons equally.

Fourth—The gasoline shortage in this area is far more critical than the average person realizes, and unless the situation eases in the next few weeks as the result of public co-operation, far more drastic restrictions, for doctors as well as for everyone else, are in the offing. No doctor should be guilty of abetting a black market under any circumstances.

Fifth—Remember we are still in an all-out war which will be won or lost by the way we fight it on the home front.

With these facts in mind you should be well guided by your conscience as you decide whether you are truly justified as a citizen aiding the war effort—not as a doctor exercising a special privilege—to use your automobile for nonprofessional driving.

CORRESPONDENCE

TAX-SUPPORTED MEDICAL CARE

To the Editor: The following letter addressed to all boards of public welfare and bureaus of old-age assistance in the State has been sent out this week. Each appointed city or town physician, and each physician who provides medical care for recipients of public assistance in any category, should obtain a copy of this formulary from the board of public welfare of the town in which he practices. The boards will greatly appreciate co-operation from physicians in the form of close adherence to the items on the formulary in their prescriptions. The boards will be able to provide physicians with any information that they may wish to obtain in regard to the formulary.

B. W. MANDELSTAM, M.D.
Medical Adviser

Department of Public Welfare
Division of Aid and Relief
State House
Boston

* * *

Gentlemen:

Administrators of public assistance have had many problems in connection with the provision of drugs for recipients of public assistance. Because of these difficulties the State Department of Public Welfare decided to compile a formulary. The formulary will be used by the department in reimbursing local boards of public welfare, but local boards will continue to deal directly with recipients, pharmacists and doctors.

The formulary has been compiled after a study of formularies of a number of hospitals, with suggestions from pharmacists as to those drugs most frequently dispensed. The list of drugs in the formulary, and the prices, have been approved respectively by the physicians' advisory committee and the druggists' advisory committee to the medical adviser of the State Department of Public Welfare.

With very few exceptions the list is composed of drugs that are standard *United States Pharmacopeia*, and not proprietary, products. Proprietary names have been listed in a number of instances, with a cross reference to the *U.S.P.* drug which is equivalent. The list has been prepared in alphabetical form for convenience. Revision will be made from time to time, depending on changes in price or on demand by physicians for additions.

The department will not reimburse local boards for drugs not on this list, unless prior approval has been obtained from the district office of the department. The price paid for any medication on the list will not be greater than the price listed therein. Every effort has been made to adjust quantities and prices so that physicians can prescribe sufficient medication to last for the whole interval between visits.

There are two types of formulary—one with prices and one without. The former is for the use of druggists who are providing medicine to recipients of public assistance. That without prices is for the use of physicians who are providing medical services to such recipients. Local boards of public welfare may secure the needed number of each type from their district office.

Where the recipient is allowed to purchase drugs from any pharmacist, or from a limited number of pharmacists, the mechanism of billing for the drugs depends on

the local board of public welfare. Arrangements should be made between the druggist and the local board for the proper method of billing the recipient or the board.

Further information will be furnished from the Department of Public Welfare through the district office.

ARTHUR G. ROTCH
Commissioner

Department of Public Welfare
State House
Boston

BOOK REVIEW

Electrophoresis of Proteins and the Chemistry of Cell Surfaces. By Harold A. Abramson, Laurence S. Moyer and Manual H. Gorin. 8°, cloth, 341 pp., with 155 illustrations. New York: Reinhold Publishing Corporation, 1942. \$6.00.

This book deals with a rapidly expanding field of investigation, which is of growing importance in medical science. The fact that charged particles (including cells, bacteria and protein molecules) move in an electric field has long been appreciated, but only recently has it been put to use through the development of the Tiselius and similar instruments. With proteins, electrophoretic methods may be used to estimate the quantities of components of different mobilities in a mixture such as plasma, to separate these components and to demonstrate the identity or heterogeneity of a chemically isolated fraction.

Many clinically useful tests (albumin-globulin ratio, sedimentation rate, Takata-Ara reaction, colloidal-gold test) depend on variations in the protein pattern. Whereas plasma albumin migrates as a unit, the globulins can be separated into at least three components, so that electrophoresis has much potential clinical value. Certain antibodies are recognized by the great increase in quantity of a protein component occurring in hyperimmune sera and by its disappearance after absorption by the specific antigen. The antibody components are identical with the gamma globulin or fall between the gamma and beta globulins on the electrophoretic diagram. Consequently, the supposition has been made that the increase in plasma gamma globulin occurring in sarcoidosis and amyloidosis may represent antibody formation. Furthermore, electrophoretic methods have been of value in controlling the separation of trophic hormones from extracts of the anterior pituitary gland and in proving their purity.

The book details many other investigations, including chapters on latex and on the surface chemistry of cells and a discussion of therapy by electrophoretic transport of drugs and allergens through the skin.

A book covering the rising curve of research in a new field can hardly be written in leisure, and suffers in being out of date before the ink is dry; and a more compendious index might have increased its usefulness. These inadequacies are small beside the value of a much-needed monograph. The first half of the book (theory and methods) is indispensable to those who undertake electrophoretic studies or the critical evaluation of those of other men. The entire book is worthy of perusal by clinicians and investigators who wish to keep abreast of the biophysical aspects of disease.

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SO CALLED "ATYPICAL PNEUMONIA" AMONG COLLEGE STUDENTS*

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THERE has recently been noted among the students at Harvard University a marked increase in the incidence of an acute infection the etiology of which is little understood. Reinmann^{1, 2} in 1939 called attention to isolated cases of a form of pneumonia in adults, apparently not caused by bacteria or by the virus of epidemic influenza. From 2 of the cases that he reported during the years 1938-1939 a filterable infectious agent was recovered. Smiley, Showacre, Lee and Ferris³ in the same year reported what they called "acute interstitial pneumonitis" in the student body of Cornell University. Murray⁴ reported a group of so-called "atypical pneumonias" occurring in Harvard students during the winter of 1936-1937. Within the past year, Finland and Dingle^{5, 6} discussed in great detail the various types of pneumonias and included in their discussion all the known pneumonias not caused by a definite bacterial infection. They reviewed the literature thoroughly for the types of pneumonia which had been more frequent in recent years and in which the pulmonary lesions were not due to the common pathogenic bacteria. They called attention to the fact that atypical pneumonia was almost entirely limited to adolescents and young adults. They also believed that little is known about the mode and manner of spread of this illness. The general consensus, they said, is that it is transmitted by contact but is not highly communicable. Although the disease is commonly referred to as "virus pneumonia," no one of these authors was able to prove or disprove that these somewhat related pulmonary diseases are due to a virus. They were all in agreement, however, that it is not of bacterial origin.

Since July, 1942, there have been admitted to the Sullman Infirmary some 75 cases of atypical

pneumonia, proved by clinical and roentgenologic evidence. No case was considered so proved unless the symptoms were fairly typical and x-ray examination of the chest showed changes compatible with atypical pneumonia. This a great increase over any number admitted in recent years. During the academic year of 1938-1939, of 2128 admissions there were 81 cases diagnosed as bronchopneumonia. During 1939-1940, of the total of 1943 patients admitted only 15 were diagnosed as having bronchopneumonia. During 1940-1941, during which time there were 2104 admissions, only 7 cases were diagnosed as bronchopneumonia. In 1941-1942, there were 15 diagnoses of atypical pneumonia among 1595 admissions. From July 1 to December 20, 1942, there were 75 cases of atypical pneumonia among some 884 admissions. This is 8 per cent of the total admissions in this period, a startling percentage indicating the high incidence of this illness at the present time.

The average age of patients in this series, all of whom were males, was twenty, the youngest patient being seventeen and the oldest twenty-four. This does not mean that the illness is confined entirely to this age group, it may occur in older persons, although perhaps with less frequency.

INFECTIOUSNESS

The question of infectiousness of this disease is most debatable at the present time. It is the belief of some^{1, 2} that it is highly contagious, but from a practical viewpoint, considering our experience during the last few months, it is surprising that none of the personnel of the institution caring for these patients have been ill although no extraordinary precautions were taken. Moreover, there was no case in which both of two roommates were afflicted with the disease. In one case, a boy who had been exposed to atypical pneumonia in an open ward was readmitted two

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weeks later with the disease. For the most part these patients were kept in the same ward as were students with ordinary respiratory infections and a mixture of other unrelated illnesses. With this experience, it is most difficult to interpret accurate-

feverishness and, rarely, extreme lethargy. In a few cases cough, although of a minor character, was present, and in some a history of a head cold of several days' duration was obtained. The onset of the disease was insidious, chest pain was absent

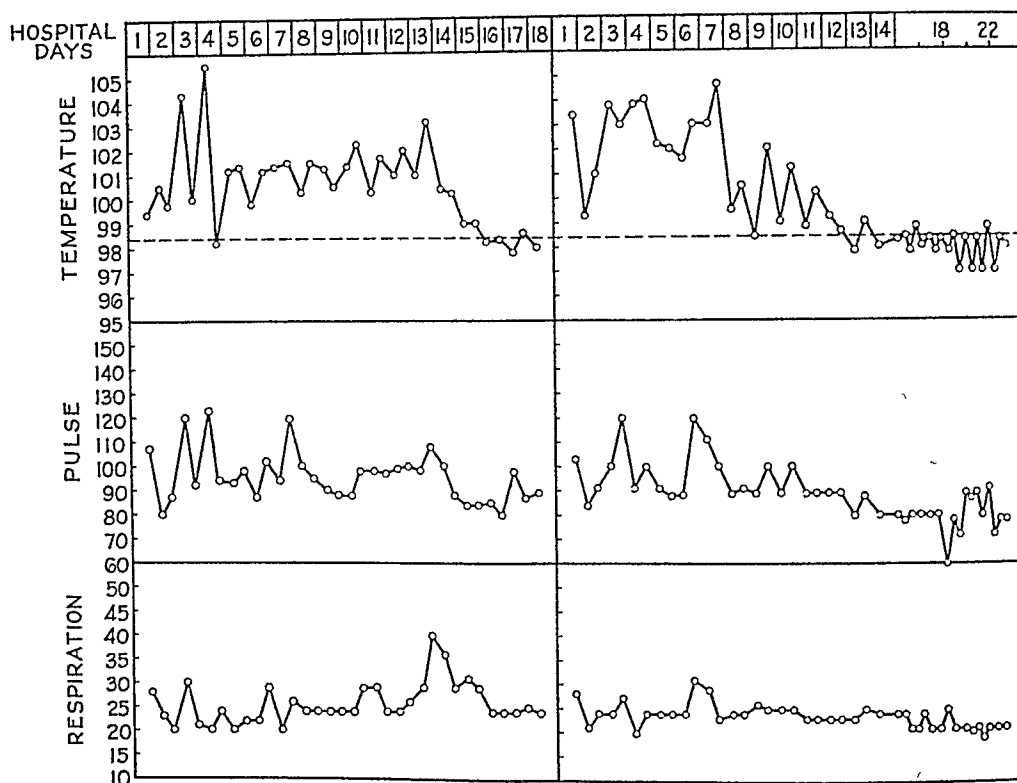


FIGURE 1. Charts of Case 1 (left) and Case 2 (right).

ly the infectiousness of the disease, and it has not seemed worth while to use infectious precautions such as are required for the handling of a highly contagious illness. It may well be that, as suggested by Bock⁷ and Reimann,² this infection is a manifestation in one patient of atypical pneumonia, whereas in another it manifests itself in a no more serious way than a "cold." On this assumption, it does not appear to be necessary to use extraordinary precautions in handling cases of atypical pneumonia when the free movement of those suffering from "colds" is permitted. The major precaution is, perhaps, the simple requirement that none of the staff shall appear on duty while afflicted with an acute respiratory infection, regardless of its severity.

SYMPTOMS

The symptoms were extremely variable but the absence in most cases of any symptoms referable to the respiratory system was noticeable. The predominating symptoms at the time of admission were easy fatigue, general malaise, muscle pains, headache, an alternate feeling of chilliness and

in all cases, and cough in the great majority of cases was absent or minor with the exception of several cases to be discussed later. In no case was there expectoration of sputum of any noteworthy amount, or of prune-juice or bloody sputum.

PHYSICAL EXAMINATION AND HOSPITAL COURSE

The physical examination at the time of admission showed an average temperature of 102°F., the lowest being 100 and the highest 104. The remainder of the examination was negative unless the student had had the illness for five to six days before admission, in which case coarse rales could be heard in some area of the lung field. The white-cell count was within the normal range with one or two exceptions, when it was 14,000 or 15,000 on the first day but was below 10,000 on the second. The initial elevation in these exceptions may have been due to dehydration. A noticeable leukopenia was absent in the great majority of cases, the lowest count being 5200 and the average 6800. The differential count and the blood smear were characteristically in the normal range. The only possible way of making a diag-

nosis in the early stages is by means of x-ray examination of the chest. In some cases the findings were normal during the first few days of the illness (Case 1) and for three or four days after admission, although the symptoms of general

usual first physical sign was the appearance of coarse rales, most often on the fifth or sixth day, but sometimes as late as the tenth. Frequently at the time of the appearance of the rales the patient was feeling better and the temperature was

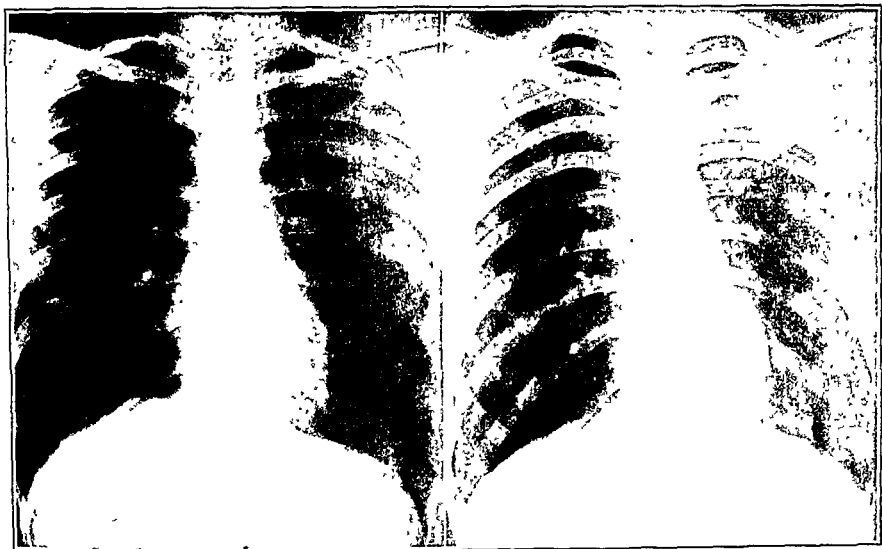


FIGURE 2 Case 1.

The film on the left was taken on the second hospital day. There is linear increased density in the left upper lobe; otherwise the chest appears normal. The one on the right, taken on the fourth hospital day, shows an area of diffuse haziness occupying the left infraclavicular region that is consistent with pneumonia.

malaise, chilliness and so forth were marked and the temperature was high.

There seemed to be no predominance as to the area involved, although generally speaking the bases of the lungs were more frequently involved than were the upper and middle lobes. The amount of consolidation shown by x-ray examination was extremely variable. In some cases, the roentgenologic examination showed only a small area of consolidation without further progression, but in others the x-ray film was most startling in its appearance—in fact, so much so that it closely resembled the picture of miliary tuberculosis (Cases 2 and 3). The x-ray appearance was in most cases that of patchy consolidation throughout the part of the lung involved, but in approximately 20 per cent of the cases it showed frank consolidation of one lobe or another (Case 4).

In all cases except those showing lobar consolidation by roentgen ray, bronchial breathing or other signs of consolidation were absent, and the

on the down grade. Dyspnea was not present in the great majority of cases, and the respiratory rate in all except a few cases was not increased beyond the point that one would expect in a patient with fever. In some cases a rapid respiratory rate was noted (Case 3), but in these patients it was due to a shallow, panting respiration rather than to true dyspnea. The shallow, rapid respiration was due largely to the fact that deep breathing or even normal chest excursion precipitated paroxysms of coughing. Cyanosis was present in only 2 cases, and then to only a moderate degree.

The average period of hospitalization was ten days, the shortest being six days and the longest thirty days. The short hospitalization of some patients does not mean that the disease was completely over in this time. Most of the patients had been ill for four or five days before admission, and in other cases they were discharged home for convalescence before they could be considered ambulatory.

symptoms being general malaise, pains in the muscles, slight chills and fever, and a mild cough. On admission, the temperature was 104°F. (Fig. 4), and physical ex-

without benefit. The first clinical signs in the chest were heard on the 6th hospital day, when signs of frank consolidation were observed at the right base. On the

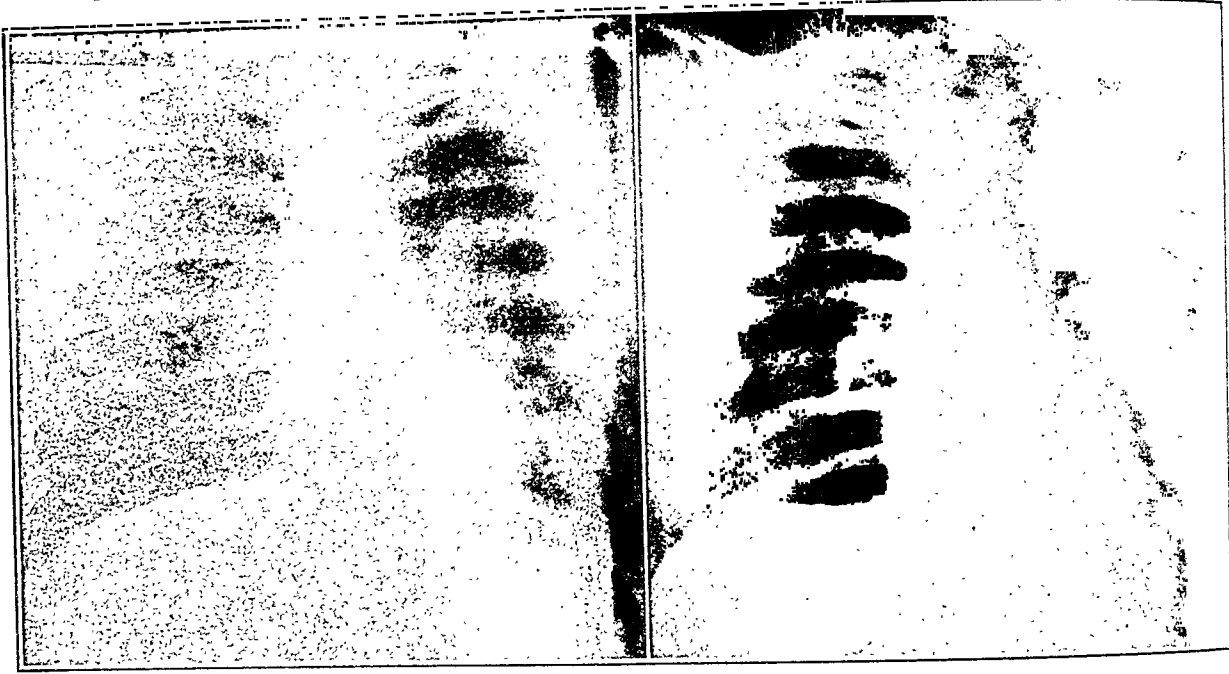


FIGURE 5. Case 3.

The film on the left, taken on the second hospital day, shows haziness in the left lower lobe lateral to the heart. That on the right, taken on the tenth day, shows a miliary process involving the entire left lung, which is most marked at the base; there is also a miliary process in the upper portion of the right lung, probably in the upper lobe.



FIGURE 6. Case 4.

This film, taken on the seventh hospital day, shows complete consolidation of the right middle lobe and of a large portion of the right lower lobe.

amination was negative; the white-cell count was 16,700, with a normal differential. A count the following day was 8000, with 90 per cent neutrophils. The patient was started on large doses of sulfathiazole 2 days after admission. This medication was continued for 3 days

following day, an x-ray film (Fig. 6) revealed complete consolidation of the right middle lobe and of a large portion of the right lower lobe. The patient continued to run a rather high temperature, which gradually subsided by lysis on the 13th hospital day. On the 18th day, moist rales at both bases were still present. The lung signs gradually abated, and the chest became clear one week before discharge. This case is most interesting in that the white-cell count continued to rise. It reached a high of 22,800 on the 13th day, when the temperature was normal. Furthermore, an eosinophilia developed, which went as high as 26 per cent. The count did not return to normal until the 32nd day, 1 week after all the chest signs had disappeared, and 19 days after the temperature had returned to normal. The cause of this queer blood picture could not be explained.

SUMMARY

A clinical study of so-called "atypical pneumonia" among 75 college students is reported. The patients were males and ranged from seventeen to twenty-four years of age, with an average age of twenty years. The average period of hospitalization was ten days, but the disability period averaged twenty-one days.

There were no serious complications and all the patients recovered without incident. Four cases, which were somewhat unusual in character, are discussed in detail, with clinical charts and roentgenologic data.

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INHALATIONAL THERAPY IN THE TREATMENT OF SERIOUS RESPIRATORY DISEASE

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THE use of oxygen for the treatment of various types of anoxemia has increased tremendously. One generally appreciates that every physiologic function is only as efficient as its supply of oxygen. Reviews of the physiologic principles on which oxygen therapy is based have been made by Haldane,¹ Haldane and Priestly,² Lundsgaard and Van Slyke,³ Peters and Van Slyke,⁴ Barcroft,⁵ Meakins and Davies⁶ and others. Reviews of its practical application have been made by Boothby and his associates,⁷⁻⁹ Barach and his associates,¹⁰⁻¹² and others.

The use of mixtures of helium and oxygen for the treatment of the various anoxemias associated with respiratory and cardiac disease has increased largely through the investigative efforts of Barach. He¹³ has repeatedly demonstrated improvement in vital capacity, marked reduction in pulmonary ventilation, diminished tidal volume, diminished residual air and increased expiratory and inspiratory velocity rates with properly directed inhalational therapy in patients with asthma and emphysema. Barach and his associates have stressed the value of oxygen and helium and oxygen mixtures with and without positive pressure in a large series of papers based on experimental and clinical observations. The use of these mixtures under positive pressure has not become so widespread as it should have. Most clinicians are discouraged by the technical details and apparatus necessary for this type of inhalational therapy. However, its value as an adjunct in the management of the desperately ill patient with respiratory disease should overcome this attitude.

Equipment for Inhalational Therapy

The following are the more commonly used methods of administering oxygen: the nasal or nasopharyngeal catheter, oxygen face masks and tents and the various types of enclosing tents.

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Each method has its special advantages and disadvantages. With the above methods oxygen can be given in concentrations of 40 to 75 per cent. With the new B. L. B. inhalation mask and oxygen flows of 5 to 12 liters per minute, very high concentrations of oxygen can be administered quite economically.

Eckman and Brach¹⁴ have described in detail the various types of apparatus that they found useful. The helium oxygen pressure apparatus is a most effective one for giving oxygen or helium and oxygen mixtures with or without positive pressure. The percentage concentrations of the mixtures can be exactly controlled. Positive pressures up to 6 cm. of water can be applied to the inner surface of the lung during both inspiration and expiration. The apparatus consists of a gas tight motor blower, two canisters for the carbon dioxide absorber, a rheostat to determine the volume of air flow and its temperature, tubal connections, an ice containing cabinet and a plastic hood in which the patient's head lies, with closure made by a soft-rubber band collar. In this rebreathing circuit only the oxygen is used up.

In a recent paper Brach and Molomut¹⁵ describe a modification of the Brach-Eckman¹⁴ mask. This new type of injector mask is metered for positive pressures up to 4 cm. of water in the expiratory phase only. Along with the injector (oxyator principle) it may be used to deliver 40 to 95 per cent oxygen or helium and oxygen mixtures with or without positive pressure during expiration. It can be used to supplement the above-described hood apparatus. The mask is a credit to the ingenuity of the authors. Both the hood and the mask apparatus were employed in the present series.

Use of Helium

Helium is an inert, colorless, odorless, non-combustible gas of low molecular weight.¹⁶ It has a specific gravity one seventh of that of nitrogen and one eighth of that of oxygen. It has a low

coefficient of solubility, being 40 per cent less soluble in water than is nitrogen. It is nearly three times more diffusible than nitrogen. Hence very little helium is dissolved or lost in the body. In comparison, nitrogen under pressure is much more soluble in body fluids and furthermore has an affinity for lipids.

In 1934 Barach¹⁷ proved the biologic inertness of helium. A mixture of 80 per cent helium and 20 per cent oxygen is one third as heavy as air. Its lightness suggested to Barach that it could be moved to and from the lungs in obstructive dyspneas more easily than air. Furthermore, a lighter-than-air mixture will go through a constricted orifice more easily. The pressure required for the movement of an 80 per cent helium and 20 per cent oxygen mixture would be about half that required for air through a similarly constricted orifice. It should be possible with helium and oxygen mixtures to compensate for approximately a 50 per cent constriction in the lumen of the tubal respiratory tract. The more localized the obstruction, the better the effect. This saving in respiratory effort may be of life-saving value.

The chief use of helium-oxygen mixtures is in the treatment of obstructive dyspnea from the larynx to the bronchiole (Barach^{17, 18} and Eversole¹⁹). It should always be given a trial in any type of respiratory obstruction in an effort to avoid tracheotomy, with its inherent complications. Helium when mixed with oxygen decreases the effort required for pulmonary ventilation, and lowering of the negative intrapleural pressure follows. Addition of positive pressure further accentuates this lowering.

The proper percentage of oxygen in the helium-oxygen mixture depends on the degree of anoxemia. The proper percentage of helium depends largely on the degree of mechanical obstruction interfering with the inflation of the alveoli. By using separate tanks, one containing 80 per cent helium and 20 per cent oxygen and the other 100 per cent oxygen, connected by a Y tube to either the hood or the mask apparatus, the desired percentage of the mixture can be changed at will to suit the patient's physiologic needs. At least 20 per cent oxygen must be administered. It is doubtful whether helium will be valuable if the mixture contains more than 33 to 35 per cent oxygen. Continuous residence in the hood may be maintained without much discomfort for many days. In one of Barach's reported cases the patient required helium-oxygen therapy under positive pressure for six days. The metered mask may be kept on for one to three days, and perhaps longer with proper rest periods. The problem of length

of residence in hood or mask varies with the degree of anoxemia, dyspnea and respiratory fatigue and the presence of psychic factors. The higher percentages of oxygen should not be used continuously, for pulmonary irritation has been described. The change from hood to mask or oxygen tent should be gradual with a progressive reduction in the percentage of oxygen, or intermittent treatment should be carried out before complete cessation.

Treatment Of Pulmonary Edema With Positive Pressure

Pulmonary edema occurs frequently in a wide range of respiratory and circulatory diseases and usually constitutes an acute medical emergency. It has been found clinically that positive-pressure inhalation of oxygen or helium and oxygen clears up the signs of pulmonary edema promptly. Barach²⁰ in his most recent paper once again demonstrated the value of properly directed positive-pressure inhalational therapy in 5 patients critically ill with pneumonia. He states that positive pressure is like putting a finger on the capillaries and stopping their oozing.

Barach²¹⁻²³ has summarized the sequence of events that follow resistance or obstruction to inspiration. There is at first a rapid and progressive increase in the intrapleural negative pressure in order to force sufficient air into the lung. Other changes, characterized by pulmonary edema and final respiratory failure, may follow. Barach and his associates^{24, 25} have repeatedly demonstrated that when oxygen or helium-and-oxygen mixtures are taken under positive pressures, the abnormally elevated negative intrapleural pressure is diminished and dyspnea is alleviated. Nature provides a helpful internal mechanism, as observed by Barach, in the severe asthmatic patient pursing his lips in expiration, and in the pneumonic patient grunting and groaning with expirations. The expiratory grunt maintains a more patent airway and helps to prevent pulmonary edema.

Properly controlled positive pressure is extremely useful in the management of pulmonary edema. The moist, bubbling rales have been seen to clear up within fifteen to forty-five minutes in a series of patients with underlying bronchial asthma, pneumonia, left-ventricular failure, mediastinal obstruction and gas poisoning. The signs of pulmonary edema usually remain absent as long as the pressure is applied or until the original cause has been removed. The application of a gentle internal distending force serves to keep the bronchioles patent and opposes the hydrostatic pressure within the capillaries.

Generally, positive pressures of 2 to 6 cm. of water are sufficient for preventing or treating

pulmonary edema Pressures above 6 cm may diminish the return flow of blood to the right side of the heart Theoretically, shock may be considered a contraindication to the use of positive pressure

Inhalation of Vaporized Bronchodilator Solutions

The value of oral inhalations of vaporized sprays of various bronchodilator solutions with the use of a hand bulb atomizer was established on a sound basis by Graeser and Rowe²⁶ Richards, Barach and Cromwell²⁷ described the technic of continuous vaporization of bronchodilator solutions for the treatment of bronchial asthma, emphysema, acute bronchiolitis and various so called "virus pneumonias" They used 1 or 2 cc of 1:100 epinephrine and 1 per cent Neo-Synephrine, alone or in combination The solution was placed in the vaporizer and oxygen was passed through it from the pressure tank at the rate of 4 to 7 liters per minute The patient simply held the nozzle of the vaporizer in his mouth and breathed quietly This therapy was repeated every three or four hours Clinical improvement was striking The vital capacity and maximum breathing capacity increased in the majority of cases

Neo-Synephrine is an effective vasoconstrictor of the mucous membrane of the tracheobronchial tree but a poor bronchodilator Refractoriness to it does not occur Epinephrine serves as an effective bronchodilator The combined effect relieves bronchial spasm and loosens tenacious mucus As a rule following such therapy the patient coughs and raises mucus and sputum that previously he could not expectorate Subjective improvement follows, and frequently the obstructive asphyxial picture is relieved after plugs are brought up from the tracheobronchial tree

This type of therapy is of greatest value in status asthmaticus It should be used, however, in all types of respiratory disease in which the mechanical factor of obstructive dyspnea due to plugging or spasm of the tracheobronchial tree exists Untoward results from such therapy are extremely uncommon If the patient is too ill to be removed from the tent or hood, the nebulizer can be passed through the tent opening or hood sleeve directly into his mouth

* * *

Based largely on the work of Barach and his associates, physiologically directed therapy in the management of patients ill with obstructive respiratory disease of varied etiology has been well established A similar program was offered successfully in a series of desperately ill patients Repeated bronchial relaxation was accomplished whenever indicated, by the use of rectal amino

phyllin, diluclid, iodides, nebulization therapy with Neo-Synephrine and epinephrine, and proper humidification High concentrations of oxygen and of helium and oxygen mixtures were given, with and without positive pressures as indicated, through the new Barach-Molomut mask and re-breathing hood apparatus The patients were critically ill and moribund at times before therapy was started The sole criterion for successful therapy was objective and subjective evidence The condition of the patients did not permit more definite studies

The present report covers the first 4 patients treated The above therapy in part or in entirety has been employed in a larger series of varying cardiorespiratory diseases and will be reported in other communications

The first patient was desperately ill with an asphyxial obstructive type of status asthmaticus, the second patient with a virulent bilateral miliary type of virus pneumonia with progressive anoxemia, dyspnea and pulmonary edema; the third patient with a bilateral virus pneumonia with underlying bronchial asthma, complicated by a massive atelectasis of the right lower lobe with mediastinal shift, and the fourth patient with a Type 7 pneumonia involving practically all the lung tissue, septicaemia, a toxic type of auricular fibrillation and other complications Progressive dyspnea, anoxemia and cyanosis had occurred in spite of the conventional methods of therapy

The program of physiologically directed therapy was begun only after all other methods had failed and the patients were desperately ill In the 3 pneumonia patients the improvement was progressive over a period of two to five days The diminished toxicity was striking after the third or fourth day The anoxemia, cyanosis and dyspnea were controllable almost from the outset of therapy The usual troublesome cough in the 2 virus pneumonia patients was controlled successfully with supplemental inhalational therapy Pulmonary decompensation was effectively controlled and convalescence was much more rapid than expected if one were to judge solely by the severity of the clinical picture

CASE REPORTS

CASE 1 The patient a 35-year-old physician, had been well except for seasonal hay fever and frequent mild upper respiratory infections until November 10 1942 On that date he complained of rhinorrhea headaches chilliness vague muscular aches and pains, and abdominal discomfort These symptoms progressed during the following 5 days On November 15 he complained of a slight cough associated with tightness through the chest and some difficulty in breathing largely in the expiratory phase The dyspnea soon became more marked, with characteristic asthmatic wheezing From November 17

to 19 the dyspnea and wheezing increased in severity in spite of barbiturates, adrenalin and intravenous aminophyllin. The chest remained fixed in inspiration and was emphysematous; over it, inspiratory and expiratory wheezes were heard, with occasional moist rales at the bases. The picture soon became that of the cyanotic, asphyxiated, obstructed, asthmatic patient.

The patient was admitted to the hospital on November 19. During the following 24 hours he was given repeated sedatives, adrenalin, aminophyllin, and helium by nasal catheter. In spite of these procedures he suffered three severe attacks of bronchospasm with an intense obstructive asphyxial picture. His condition was desperate. On November 21 he was placed in a helium-oxygen hood rebreathing apparatus and was given a mixture of 80 per cent helium and 20 per cent oxygen under positive pressure. This proved to be the turning point in therapy and the patient was soon able to get his first rest. He remained in the hood for 2 days. This therapy was further supplemented by the intermittent inhalation of mixtures of 1 per cent Neo-Synephrine and 1:100 epinephrine with 100 per cent oxygen. In addition he received dilauidid, aminophyllin by the rectal route, and supportive intravenous saline and glucose.

Under this program the patient soon improved. His cough became productive of large plugs of mucus. The dyspnea, cyanosis and anoxemia were properly controlled by varying the helium and oxygen percentages. The lung fields cleared progressively. A chest film taken on November 23 suggested emphysema, a plugged bronchus on the left and a mediastinal shift toward the right. After a few days the patient was able to get along without further helium therapy, but the inhalation sprays were continued for 3 days.

The patient was discharged from the hospital on November 29. The lung fields were clear throughout but hyper-resonant. The white-cell count and the percentage of eosinophils were still elevated, however. During the following 10 days at home he continued to complain of intermittent rhinorrhea and mild attacks of tightness through the chest, with slight wheezing. This was usually accentuated by overexertion and exposure to cold, dust or tobacco smoke. A repeated chest film was essentially normal except for slight emphysema and accentuated bronchial markings. The final diagnosis was acute upper-respiratory infection and status asthmaticus with intense dyspnea, anoxemia and cyanosis.

Comment. This desperately ill patient recovered under a physiologically directed program consisting of helium-and-oxygen mixtures under positive pressure, and inhalational sprays of Neo-Synephrine and epinephrine with oxygen. The relief from the dyspnea and anoxemia was most striking from the outset of this program.

CASE 2.* The patient, a 35-year-old, unmarried woman with an uneventful past history, became ill on December 2, 1942. At onset she complained of aches and pains, malaise, shaking chills and fever. During a 10-day period at home persistent cough, fever up to 105°F., progressive cyanosis and dyspnea characterized her course. There was no chest pain or rusty sputum. In spite of the giving of oxygen by facial mask and sulfadiazine, difficulty with respiration and anoxemia progressed. The patient was seen by Dr. Maxwell Finland in consultation and removal to the hospital was advised.

*This case is reported through the courtesy of Dr. Maxwell Finland.

On admission on November 12, the patient was acutely ill, dyspneic, dehydrated, drowsy, incoherent and cyanotic. The temperature was 101°F., the pulse 120, and the respirations 30. The respiratory movements were rapid and shallow. The lungs revealed a variety of expiratory squeaks and medium to coarse rales, largely limited to the top of both lungs anteriorly and the lower half of both lungs posteriorly. The abdomen was distended and the urinary bladder full. The white-cell count was 16,200, with 86 per cent polymorphonuclear leukocytes and many toxic granules. The red-cell count was 4,460,000 and the hemoglobin 65 per cent.

The admission diagnosis was bilateral atypical pneumonia. Chemotherapy was discontinued, and oxygen was given by nasal catheter and later by mask, and fluids by clisis and general supportive care. A sputum culture later showed many colonies of staphylococci by direct inoculation on blood agar. Sulfadiazine was resumed on December 16. An x-ray film revealed a bilateral, diffuse, miliary type of virus pneumonia.

During the 1st week in the hospital the patient's course was characterized by progressive dyspnea, cyanosis, abdominal distention and periods of irrationality and urinary incontinence. The temperature remained between 101 and 103°F., the respirations at 48 and the pulse at 120 to 140. On the 16th day of illness the patient's condition was desperate and a program of positive pressure with oxygen and helium-oxygen mixtures was finally begun.

For 15 hours a B. L. B. mask was arranged to give positive pressure in the expiratory phase of respiration, with flows of 10 to 12 liters per minute of oxygen or helium-oxygen mixtures. The respiratory rate was slowed and the patient managed to get a few hours of rest during the first night. On December 19 a new Barach mask metered for positive pressure was used and this was continued for 5 hours. The patient was then placed in a helium-oxygen hood. It is significant that the respirations had dropped to 28 before entering the hood, and that gurgling and bubbling rales heard over the top of both lungs cleared up promptly with positive pressure.

The patient remained in the hood for 3½ days, and had her first hours of comfortable sleep there. During this time she received mixtures of helium and oxygen in varying percentages depending on the anoxic or obstructive factor. In addition she received inhalational sprays of mixtures of 1 per cent Neo-Synephrine and 1:100 epinephrine every 4 hours, with flows of oxygen of 4 to 6 liters per minute. The mixture was generally introduced through the sleeve of the hood, with the nurse holding the nebulizer in the patient's mouth or the patient holding the nebulizer between her lips. Further therapy consisted of 1/64 gr. of dilauidid twice daily as needed, and potassium iodide orally. The abdominal distention was strikingly relieved at the onset of therapy when the patient received straight oxygen. Sulfadiazine was stopped on December 20 because of diminished urinary output. At various times definite prolonged expiratory wheezes were elicited over both lung fields.

The general course was one of slow but progressive improvement. While the patient was in the hood the temperature ranged around 99.6°F. rectally, the pulse between 96 and 112, and the respirations between 28 and 32. She was considerably less toxic. Her color remained pink and breathing was not labored.

The cough soon became productive. The sputum was at first sticky and glairy, and later less tenacious. After $3\frac{1}{2}$ days in the hood she returned to the Barach-Molomut mask with positive pressure of 4 cm in the expiratory phase only, using largely 95 per cent oxygen alone. This was continued for 2 days and thereafter intermittently for 6 days. During these periods the percentage of oxygen was slowly reduced. Nebulization therapy was continued, however, until December 31. Scattered medium moist rales could still be elicited at the bases posteriorly on January 2, 1943, the day the patient was allowed up in a chair. She shortly became ambulatory and was discharged home to convalesce on January 5. During the first 2 weeks at home she had two attacks of sudden breathlessness at night, relieved by Propadrine Hydrochloride. Scattered expiratory wheezes could be elicited. This bronchospasm soon cleared up however.

Comment. A desperately ill patient with bilateral virus pneumonia, unresponsive to usual methods of care, responded characteristically to a program of physiologically directed inhalational therapy consisting largely of mixtures of helium and oxygen under positive pressure. The most striking observation was the relief from cerebral anoxemia and respiratory failure which appeared imminent at the beginning of therapy.

CASE 3.* The patient, a 25-year-old intern with a past history of autumnal asthma, was admitted to the hospital because of a 4-day history of sore throat, headache, malaise, anorexia, abdominal distress, fever, substernal tightness and nonproductive cough.

Physical examination revealed a flushed, perspiring young man with slight expiratory wheezing. The temperature was 101°F , the pulse 86, and the respirations 24. The outstanding findings were in the chest, which was increased in the anteroposterior diameter, with the breath sounds distant. There was slight dullness at both bases, with bronchovesicular breathing but no rales. In constant wheezes were heard throughout both lung fields. A chest film revealed haziness in the right lower and left lower lung fields.

The laboratory data revealed a slightly elevated white cell count. Throat, sputum and blood cultures were negative for pneumococci.

The diagnosis on entry was an atypical pneumonia. The patient was treated symptomatically. In the course of the first few days the temperature rose to between 102° and 104°F . On the 6th day, because of failure to respond and because of increasing signs of consolidation, he was given full doses of sulfadiazine. Nevertheless there was a gradual rise in pulse and respiratory rate and no drop in temperature. Paroxysms of nonproductive coughing then developed accompanied by cyanosis and exhaustion. Both the clinical and x-ray impressions were those of an extensive pneumonia involving the entire right lung and the left lower lung. The mediastinum was shifted to the right and there was apparently some degree of atelectasis of the right lower lobe. At times there was definite evidence of bronchospasm only partially relieved by epinephrine.

The clinical course was progressively downhill with increasing anoxemia, cyanosis and dyspnea in spite of oxygen therapy with the B. L. B. mask and oxygen tent. On December 27 the patient appeared desperately ill. Loud bubbling rales were heard throughout both sides

of the chest in both phases of respiration, with marked lengthening of expiration. A program of therapy was begun consisting of nebulizer inhalations of epinephrine and Neo-Synephrine, rectal aminophyllin and positive pressure helium-oxygen mixtures. Within 15 minutes after the patient was placed in the hood under positive pressure the bubbling rales disappeared and the respirations became easier. He soon fell asleep and awoke in an hour considerably refreshed.

He remained in the hood for $4\frac{1}{2}$ days. Nebulization was generally carried out while in the hood. The mixtures of helium and oxygen varied depending on the degree of cyanosis and respiratory obstruction. The toxicity diminished strikingly and the temperature began to return to normal after the 3rd day. The pulse and respiratory rates became slower shortly after this program of therapy was begun. The troublesome cough was more easily controllable, less distressing and more productive. After residence in the hood the patient was placed in the Barach-Molomut mask with varying percentages of oxygen under positive pressure. These percentages were gradually reduced, and oxygen therapy was stopped on January 1, 1943. Nebulization therapy was continued for a few more days. He was permitted up on the 24th hospital day and was discharged home on the 30th day. The final diagnosis was bilateral atypical pneumonia with atelectasis of the right base and a mediastinal shift to the right, and acute bronchospasm.

Comment. A seriously ill patient unresponsive to the usual methods of care, responded characteristically to a program of inhalational therapy consisting largely of mixtures of helium and oxygen under positive pressure.

CASE 4.† The patient, a 44-year-old, married man, had had a chronic upper respiratory infection for 1 month prior to the present illness. Three days before hospital entry there occurred the sudden onset of marked malaise, repeated chills with high fever, cough productive of blood streaked sputum and pleuritic pain in the right lower chest. In the past a mild hypertension and renal lithiasis had been observed.

The admission physical examination revealed a markedly dyspneic, cyanotic, toxic and dehydrated middle-aged man. The temperature was 104°F , the pulse 120 and the respirations 30. There was dullness at both lung bases with diminished breath sounds and moist rales. The cardiac examination revealed no murmurs or enlargement. The rhythm was regular. The blood pressure was 140/70. The laboratory examination revealed a Type 7 pneumococcus in the sputum and also in the first blood culture. The white-cell count was 17,700, with 82 per cent polymorphonuclear leukocytes. The hemoglobin level and red-cell count were within normal limits. A urine examination was entirely negative and showed a specific gravity of 1.029.

The admission diagnosis was lobar pneumonia and septicemia due to a Type 7 pneumococcus. The patient was started immediately on 4 gm of sulfadiazine, with 1 gm every 4 hours thereafter. During the first 4 days the temperature varied between 102° and 104°F , the pulse between 110 and 130 and the respirations between 25 and 30. On the 5th day the temperature climbed to 105°F , the pulse to 150 and respirations to 40. X-ray studies revealed an extension of the process from the right base to the right upper lobe. The blood sulfadiazine level

*This case is being reported through the courtesy of Drs. Harry L. Nenthal and H. J. Blumgart.

†This case is reported through the courtesy of Dr. Hyman Meertson.

was 9.0 mg. per 100 cc. The patient was extremely anoxic and demonstrated a moderate degree of expiratory stridor in spite of oxygen therapy with both B. L. B. and Barach-Eckman masks. He was then given a Type 7 antipneumococcus serum—150,000 units on the 1st day and 270,000 units on the 2nd day. Because of the persistence of anoxemia, cyanosis and mental confusion and the appearance of respiratory fatigue, a program of positive-pressure oxygen was agreed on. The patient was first placed in the hood rebreathing apparatus, with 100 per cent oxygen under positive pressure of 2 to 5 cm. of water. He remained in the hood most of the time during the following 4 days. During the rest of the time this program was continued in the Barach-Molomut mask. The temperature fell gradually during these 4 days and the respirations were much less labored. Cyanosis and anoxia were much less evident. However, auricular fibrillation developed with a radial rate of 150. The white-cell count rose to 56,000, urine examinations revealed albuminuria with a fixed specific gravity of 1.010, and the nonprotein nitrogen rose to 81 mg. per 100 cc. The patient presented signs of upper abdominal distention, which was relieved with a Levine tube and gastric lavage. Positive-pressure oxygen was discontinued on the 5th day after all signs of respiratory fatigue and tracheal rales had subsided. Oxygen therapy was continued, using the Barach-Molomut mask with mixtures of oxygen varying from 80 to 90 per cent depending on the degree of anoxemia.

The auricular fibrillation was controlled by digitalis. Because of the findings of renal insufficiency, chemotherapy was omitted. During the next week the temperature again began to rise slowly in a fluctuating fashion, reaching 103°F. X-ray examination revealed persistence of signs in the right upper and middle lobes. The white-cell count gradually dropped to 14,000 and the nonprotein nitrogen fell to 61 mg. per 100 cc. The urine showed persistent albuminuria, with specific gravities averaging 1.010. In the terminal 5 days progressive disorientation and confusion developed. Because of the cerebral symptoms it was thought advisable to continue the oxygen therapy in the oxygen tent. During the last 24 hours in spite of this therapy the patient developed rapid pulmonary edema and respiratory failure and died on January 31.

The autopsy revealed massive bilateral pneumonic involvement, with bronchiectatic abscesses in the right base, diffuse fatty infiltrative changes in the renal tubules and an acute bacterial endocarditis (terminal, Type 6 pneumococcus).

Comment. A desperately ill 44-year-old man with a Type 7 pneumonia and septicemia developed progressive signs of anoxemia, cyanosis and respiratory fatigue in spite of the usual methods of oxygen administration. These were adequately controlled during a 4-day period with a program of positive-pressure oxygen. However, progressive signs of renal insufficiency, cerebral psychosis and pneumonia spread and acute bacterial endocarditis resulted in death.

SUMMARY

A report is made of the use of positive-pressure inhalational therapy with mixtures of helium and oxygen and oxygen alone in the treatment of 4 patients desperately ill with respiratory disease.

The importance of supplemental inhalational therapy of mixtures of Neo-Synephrine and epinephrine, vaporized with a continuous flow of oxygen, is demonstrated.

Helium-oxygen and oxygen mixtures under positive pressure have a definite value in the therapy of pulmonary edema of varied etiology, bronchial asthma, acute bronchiolitis, acute fibrinous tracheo-bronchitis, severe emphysema, pulmonary fibrosis, laryngospasm, laryngeal diphtheria with obstruction, severe obstructive whooping cough and certain pneumonias or gas poisonings.

All cases of obstructive respiratory disease demonstrating anoxia, cyanosis, asphyxia, pulmonary edema or progressive intractable dyspnea, alone or in combination should have a trial with the above therapy.

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TOXIC PSYCHOSIS AND DEATH ASSOCIATED WITH POTASSIUM THIOCYANATE THERAPY*

Report of a Case

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THE purpose of this article is to emphasize the toxicity of potassium thiocyanate and to present a case showing acute psychosis with a fatal outcome.

The literature contains many reports concerning the use of potassium thiocyanate, the most notable early references being those of Pauli¹ in 1903 and 1904, who first noted its hypotensive effect; Westphal² in 1926, who reawakened interest in the therapeutic possibilities of the drug; and Barker³ in 1936, who first emphasized potassium thiocyanate blood levels as a method of control of therapy.

The pharmacologic and therapeutic properties of this drug were first reviewed in 1925 by Nichols,⁴ who observed that it was highly toxic for guinea pigs, and that a few hours after administration of the drug there developed diarrhea, progressive loss of weight, marked evidence of spinal irritation, convulsions, coma and death. His experiments appeared to substantiate Bernard's original claim that potassium thiocyanate is a tissue poison.

A total of 9 fatalities have appeared in the literature. The first fatal case, reported by Lesser⁵ in 1898, was that of a magician who took the drug with suicidal intent. Death occurred within ten hours, and an autopsy revealed extensive necrosis and hemorrhage in the mucous membrane of the gastrointestinal tract. The second case, reported by Kobert⁶ in 1906, was that of a woman who died twenty-eight hours after ingestion of this drug. There is some hesitancy in including this among the lethal group because of the inordinately small total dose of the drug allegedly taken (5 gr.). In

1916, Vintilesco and Popesco⁷ reported a toxic psychosis with delirium, convulsions, spinal rigidity, coma, anuria and death in two days after the intake of an estimated 100 gm. of potassium thiocyanate. Healy⁸ in 1931 reported 2 cases in each of which the patient had taken a total of 9 gm of potassium thiocyanate for therapeutic purposes. In one case the lowering of the blood pressure was followed by marked weakness, collapse, semi-coma and death nineteen days after discontinuance of the drug. In the other case death occurred two weeks after discontinuance, following a similar train of symptoms. Goldring and Chasis⁹ mentioned 2 additional fatal cases, again associated with the therapeutic administration of potassium thiocyanate. In these cases there was an acute outbreak of mental symptoms, particularly confusion, incoherence, hallucinations and delirium, followed by excessive psychomotor activity, anuria and death. The last 2 cases reported were those of Garvin¹⁰ and Russell and Stahl,¹¹ both with pictures of toxic psychosis, overactivity and death. The latter authors emphasized the following characteristic clinical syndrome in mortal cases: first, there may be weakness (possibly due to lowering of the blood pressure), then outbreak of an acute toxic psychosis that primarily presents delirium, confusion, hallucinations and signs of irritation of the central nervous system. In all cases in the literature death has occurred within nineteen days after the onset of the first symptoms. It is to be noted that the two blood levels recorded in association with the fatal cases were only 18.7 mg. and 21.6 mg. per 100 cc., and that in 1 case the total drug ingestion was as little as 5.6 gm., the patient receiving only 0.4 gm. (6 gr.) per day for fourteen days.

Although it is quite clear that in fatal cases symptoms of mental disorder are prone to precede exodus, mental symptoms in the course of potassium

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thiocyanate therapy are by no means limited to fatal cases. Toxic central-nervous-system symptoms have been stressed from the earliest days of the use of the drug. McNeill¹² (1933), using it for the reduction of hypertension in state-hospital patients, noted in 4 out of 12 cases unsteady gait, confusion and rambling talk resembling that of an acute alcoholic intoxication. The mental reaction lasted for four to eight days after withdrawal of the drug. In 11 of 50 cases treated by Goldring and Chasis,⁹ the usual order of toxic symptoms was muscular fatigue associated with nausea, vomiting, disorientation and mental confusion, then frequently motor aphasia and hallucinations of sight and hearing. In ambulatory cases, they noted that the muscular fatigue was first complained of, but in bed patients this early warning of toxicity might pass entirely unnoticed, and it was not unusual for motor aphasia, mental confusion and even hallucinations to be the first sign of potassium thiocyanate intoxication. These authors believed that the toxicity was not especially a function of the dosage used. Other writers have stressed the fact that there may be markedly varying rates of excretion of potassium thiocyanate in different patients. Some are distinctly susceptible, and in some there is little or no margin of safety between the therapeutic and the toxic dose. Blood levels afford comparative safety in the control of therapy, yet cases have been reported of toxicity at supposedly safe levels (8 to 12 mg. per 100 cc.).

With regard to the manner in which potassium thiocyanate exerts its effects on tissues, the experiment of Robinson and O'Hare¹³ is noteworthy. By use of the Warburg apparatus, it was found that slices of liver exposed to potassium thiocyanate in a serum medium suffered a reduction of oxygen consumption of 40 per cent when the potassium thiocyanate concentration was 20 mg. per 100 cc. They suggest that there is probably a continuous moderate reduction of metabolism in all tissues. It is possible that nervous tissue and kidney tissue—in view of uremic exodus in several cases—are especially vulnerable.

CASE REPORT

W. S., a 46-year-old, married Negro, was admitted to the Boston Psychopathic Hospital on September 30, 1942, because of delusions and confusion. From the end of World War I, in which he saw military service, until his illness, he was employed as a letter carrier. He was known as a hard, steady worker and had no bad habits. Except for "pleurisy" of short duration each winter, he had been essentially without complaints.

In the spring of 1940, however, the patient was admitted to a hospital for the first time because of progressive dyspnea, chest pain and loss of weight of several months' duration. Physical examination at that time revealed

essentially a well-developed individual, moderately obese but not acutely ill. There was an arcus senilis arterio-venous nicking of the retinal vessels, elevated blood pressure (210/130) and slight cardiac enlargement, both clinically and by x-ray. An electrocardiogram strongly suggested coronary thrombosis with myocardial infarction. Laboratory analysis revealed normal blood, a nonprotein nitrogen of 40 mg. per 100 cc., a negative urine and adequate renal function by a dye-excretion test (phenol-sulfonephthalein). On bed rest and digitalization, the patient improved and after 1 month's hospitalization was discharged with a diagnosis of hypertensive arteriosclerotic heart disease.

For 2 years the patient was well and able to continue with his work, but in August, 1942, he again complained of shortness of breath, aggravated by exertion, and was readmitted to the hospital. At that time he was coughing, with production of occasional brownish sputum, and the left lower chest showed dullness. There was no peripheral edema. The blood pressure was 242/140. The heart was enlarged to the right and left as shown by x-ray, and an electrocardiogram revealed evidence of an old anterior-wall infarction. The blood was normal, and serologic tests for syphilis were negative. Urine examination showed persistent albuminuria (30 to 50 mg. per 100 cc.) and a low specific gravity (1.008 or less) on random specimens. The nonprotein nitrogen was 45 mg. per 100 cc.

The patient was put to bed. On August 14, potassium thiocyanate therapy was begun, 3 gr. three times a day, and a blood level of 8 to 9 mg. per 100 cc. was subsequently obtained. One and a half grains of digitalis three times a day was given for three days, followed by 1½ gr. daily. There was gradual disappearance of the cough and brownish sputum, and improvement of the dyspnea. On September 23, the 40th day of treatment, the patient was allowed out of bed. The blood pressure all this time had maintained itself around 210/130. On September 25, the potassium thiocyanate was discontinued. On September 30, the patient developed delusions that he was being shunned by everyone and was being threatened. He wandered about looking for a gun to protect himself. He was violent, overactive and disoriented and was transferred the same day to the Boston Psychopathic Hospital.

The mental status revealed an inattentive, perplexed, preoccupied patient who stared about in bewilderment. He gave his family history fairly coherently but was unable to tell the year of his marriage, the ages of his sons or what he had recently eaten. He could not give the date or the name of the hospital. He had no memory of the events that had led to his admission. His retention of digits was exceedingly poor, and his range of general information was inadequate.

About 12 hours after admission, the patient began to wander about the ward praying loudly and fervently, and exposing himself. He became resistive and combative and failed to grasp the significance of his surroundings. On October 2, blood studies revealed that the potassium thiocyanate level was 18.9 mg. per 100 cc. and the nonprotein nitrogen 70 mg. During the next few days the patient went rapidly downhill, showing excessive psychomotor activity and requiring constant restraint. He developed coma and increasing uremia. On October 8, at which time the potassium thiocyanate level was 24 mg. per 100 cc. and the nonprotein nitrogen 130 mg., he suddenly died. Death occurred on the 55th day after

the beginning of potassium thiocyanate treatment, 14 days after the drug was discontinued, and 9 days after the onset of mental symptoms. The total amount of the drug administered was 25 gm

COMMENT

Essentially, this patient had a past history of hypertension and two episodes of congestive failure requiring hospitalization. On the second hospitalization, it was evident that he had developed albuminuria and a low urinary specific gravity. After several weeks he was sufficiently improved to be up and about. He had received treatment with potassium thiocyanate for forty-two days and it was then omitted because of his improvement. Five days later, however, he suddenly developed a toxic psychosis, went downhill rapidly, showed excessive psychomotor activity and died in uremia. Potassium thiocyanate levels taken two days after the onset of psychosis were elevated beyond the therapeutic range.

In cardiovascular renal disease, death from uremia is not uncommon. In this case the patient was markedly improved with treatment but suddenly took a dramatic turn for the worse. This course of events may conceivably occur in uncomplicated cardiorenal disease, but it seems quite likely that in the present case potassium thiocyanate intoxication played a significant part in the slump and ultimate death. This is also suggested by the sudden appearance of toxic psychosis while the patient was presumably getting well, and by the marked resemblance of the whole picture to that observed in cases of potassium-thiocyanate intoxication described in the literature. This syndrome some authors regard as characteristic of fatal poisoning. It is difficult to evaluate the exact part played by the potassium thiocyanate, and indeed it is possible that several factors are operative, including the renal impairment, elevated potassium thiocyanate blood level and special tissue vulnerability. There is not yet full understanding of the sudden elevations in the blood levels of potassium thiocyanate that can occur not only in patients who receive constant doses of the medication, but even—as in this case—after the drug has been discontinued.

In view of the experience thus far, it seems important to bear in mind the dangers inherent in

the use of potassium thiocyanate and the possibility of fatality if the drug is used in the presence of renal impairment. Acute psychosis in the course of treatment should also be regarded as a danger signal.

SUMMARY

A case of acute toxic psychosis and death associated with potassium-thiocyanate treatment of hypertension is described, being the tenth case of this type to be reported in the literature.

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MEDICAL PROGRESS

REGIONAL ANESTHESIA*

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IN THE current progress of regional anesthesia three new developments are outstanding. They are continuous caudal anesthesia for obstetrics, the subarachnoid injection of ammonium sulfate for the relief of intractable pain and refrigeration anesthesia (cryoanesthesia). However, because the anesthesiologist of today is interested in many things other than merely rendering patients insensible to pain during an operation, sections on new drugs, local anesthesia, spinal anesthesia, supportive treatment, complications and military anesthesia are included in this report.

CONTINUOUS CAUDAL ANESTHESIA

The idea of painless childbirth has been an enchanting one to anesthetists as well as to mothers since the introduction of chloroform. Continuous caudal anesthesia is the latest method holding forth this promise to appear on the anesthesia horizon. Manalan,¹ in August, 1940, introduced a technic that could have been but was not used for the continuous production of caudal anesthesia. He inserted a 13-gauge needle in the sacral hiatus and passed a No. 4 nylon ureteral catheter in through the needle, withdrawing the latter and leaving the catheter in place. After labor had progressed to the point that caudal anesthesia was needed, he injected 30 cc. of an anesthetic solution through the catheter into the sacral cavity and withdrew the catheter.

Hingson, Southworth and Edwards,²⁻⁴ impressed with the possibility for the use of the equipment described by Lemmon⁵ for continuous spinal anesthesia, adapted this apparatus (a malleable needle, tubing and syringe connected by Luer-Lok connections) for the production of continuous caudal anesthesia for obstetrics. The type of needle has been changed as dictated by their experience, as some of the original needles broke in situ. Adams and his co-workers⁶ have reported the use of a ureteral catheter by the method described by Manalan to obviate the possibility of breaking needles and to inject their agent through the catheter to produce continuous anesthesia. Several years after this method has been given a critical trial in in-

stitutions throughout the country, a worth-while evaluation of its place in obstetrics will be forthcoming. Any attempt at this stage of development to apply continuous caudal anesthesia routinely in all obstetric cases is apt to bring about some undesirable results. Southworth, Edwards and Hingson⁷ point out the possibilities of this method in certain types of general surgery, as well as in obstetrics.

RELIEF OF INTRACTABLE PAIN

Rovenstine and Wertheim⁸ make a plea for anesthetists to familiarize themselves with the various nerve blocks to provide pain relief for patients suffering from trigeminal, brachial-plexus and cervical-plexus neuralgia, sciatica, coccygodynia and shoulder pain. They advocate alcohol block of the sympathetics by the paravertebral route for angina pectoris and thrombophlebitis. Sensory-nerve block with alcohol for pain relief in inoperable carcinoma has been extremely worth while in their hands. These procedures are done only after medical treatment has failed to relieve pain or when surgical transection of sensory pathways is considered a grave hazard. Allen and Tuohy⁹ report that somatic pains can be successfully relieved in many cases by local anesthetization.

Bates and Judovich¹⁰ in an attempt to relieve intractable pain have administered 3000 injections of ammonium-salt preparations by the paravertebral route and by local infiltration. Starting with an extract of the pitcher plant (*Sarracenia purpurea*), the active principle of which they concluded was the ammonium ion, they now use ammonium sulfate. At present they inject it subarachnoidly in an attempt to control all types of intractable somatic pain. They state: "Intraspinal ammonium sulfate did not yield satisfactory results in the so-called 'pre-metastatic' phase of malignancy. The complaints of burning, urgency, tenesmus and other pains of this period were not relieved." At the time of injection, severe pain is experienced in the area supplied by nerves bathed by this solution. This can be eliminated, they state, by preceding the injection with 50 mg. of procaine hydrochloride, which provides a short period of spinal anesthesia.

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

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Hand¹¹ used ammonium sulfate subarachnoidly by the method described by Bates and Judovich in an attempt to relieve 48 patients of their intractable pain. Thirty-two of these patients had metastatic malignancy, and in 16 the treatment was successful. Six of 7 patients suffering from painful spinal-cord arachnoiditis had relief of pain. Four patients who had become addicted to morphine before treatment was instituted and 4 additional patients whose pain was finally thought to be on a functional basis received no relief. Hand thought that the major difficulty with this procedure was the inability to predict the outcome of the treatment before it was instituted, since he found it impossible to differentiate somatic pain as defined by Bates and Judovich.

Three minor complications usually accompany this treatment. First, 70 to 80 per cent of the patients experienced nausea and retching during the induction of anesthesia. This nausea could be relieved or attenuated by intravenous injections of 1/100 gr. of atropine sulfate. Secondly, 50 to 60 per cent experienced a post-spinal headache. Thirdly, 20 to 30 per cent were annoyed by varying degrees of paresthesias over the buttocks and sacrum.

REFRIGERATION (CRYOANESTHESIA)

In 1939, after long and careful study of the effects of resistance of peripheral tissue to asphyxia at various temperatures, Allen¹² suggested the possible usefulness of maintaining life processes at a reduced rate by lowering the temperature. Radical chilling of the body had previously been introduced by Fay¹³ for the cure of cancer, but he also described dramatic control of infections, including gas gangrene. True refrigeration anesthesia was first used for amputations of partially gangrenous extremities of patients in the older age group. When a tourniquet is applied and the extremity packed in ordinary chipped ice (without salt), the oxygen demands are reduced sufficiently (13 per cent for each degree centigrade) to prevent necrosis for many hours. The skin temperature falls to 2 to 4°C. and surgical anesthesia is complete within about two hours. From the anesthesia standpoint, this is thought to be an entirely new principle, namely anesthesia of protoplasm, in contrast to all former methods, which produce only anesthesia of nerves.¹⁴

Theoretically, one might expect that the tourniquet and refrigeration would increase the dangers of postoperative slough. Practically, it has been found that the factors of safety in this respect are quite adequate even in the presence of arterial disease. One report of 58 amputations done with

this type of anesthesia gave the following as its benefits: ease and quickness of operation, absence of pain both before and after operation, inhibition of infection, conservation of poorly nourished tissues, control of edema, promotion of drainage when necessary, probable reduction of thrombotic and embolic dangers and, 'pre-eminently, the avoidance of shock'.^{15, 16}

McElvenny¹⁷ used intensive refrigeration without a tourniquet to control pain, to prevent infection and to overcome shock in a patient who had bilateral traumatic leg amputations.

Refrigeration anesthesia seems to offer advantages for nearly all cases of severe wounds of the extremities. Prevention and treatment of shock may be sufficient indications; surgical anesthesia is a valuable by-product. It has been advocated for use in combat areas by military surgeons to relieve the suffering and blood loss from periodic loosening of an emergency tourniquet.¹⁸

NEW DRUGS

In 1939, Eisleb and Schaumann¹⁹ introduced a new synthetic phenyl-piperidine derivative, Demerol (1 methyl, 4 phenyl-piperidine, 4 carboxylic acid ethyl hydrochloride), which was found to possess properties similar to those of atropine and morphine. Since then numerous European investigators have attested to the drug's usefulness in the therapy of pain.²⁰ Batterman²¹⁻²³ studied the analgesic effectiveness, potency and safety of Demerol, and concluded that it could be used for patients who would ordinarily require opiates. He found the drug similar to morphine in its analgesic action and approaching it in effectiveness, but with less depression of the central nervous system. Unlike morphine, depression of the respiratory rate and urinary retention are rare following therapeutic doses. The size of the pupils and the pupillary reflexes are not affected, and in recumbent subjects there is no appreciable alteration in blood pressure, ventricular rate, electrocardiogram or basal metabolic rate.

Climenko and Berg²⁴ in a study of the influence of Demerol on the contraction of the ureter concluded that it inhibits the amplitude of contraction and diminishes the tonus of the ureter.

Rovenstine and Batterman²⁵ studied this drug to evaluate its effectiveness as a preanesthetic agent in man and to determine the differences between its action and that of morphine. They concluded:

[Demerol] will provide psychic sedation not surpassed by morphine; will not depress respiration or other vital functions to the same degree as will comparable amounts of morphine; will facilitate induction of anesthesia as does morphine; is more effective in

drying secretions than morphine; has fewer unfavorable side effects, such as nausea and vertigo, than morphine; and will reduce the amount of anesthetic agent required to produce the optimal degree of narcosis to the extent that can be obtained with morphine.

In 1937, the synthesis of monocaine hydrochloride (mono-isobutyl-aminoethyl-para-aminobenzoate hydrochloride), an isomer of procaine, was reported by Goldberg and Whitmore,²⁵ who claimed that it was a good local anesthetic with pressor action and synergistic with epinephrine. They also stated that a 1 per cent concentration could be used without the addition of epinephrine. After extensive investigation designed to test the local anesthetic efficiency of monocaine, its possible direct vasoconstrictor power, its local and systemic toxicity and its effects on vital function, Schamp, Schamp and Tainter²⁶ reported the following:

These results taken together indicate that the local anesthetic efficiency of monocaine is similar to that of procaine quantitatively and qualitatively, as is also the systemic toxicity, except for a greater cardiovascular paralyzing action of monocaine. They also fail to substantiate current claims that monocaine is a pressor agent, or that it potentiates the action of epinephrine. Since monocaine is definitely more irritating to tissues than procaine, it lacks the advantages which would justify its selection over procaine as a local anesthetic for injection purposes.

The formic acid salt, monocaine formate, which is soluble in any dilution needed clinically, was used by Burdick and Rovenstine²⁷ for a clinical study of the drug as a spinal anesthetic agent. They used technics for administration commonly employed for spinal anesthesia with procaine, dissolving the monocaine formate crystals in the spinal fluid to make concentrations of 2.5, 5.0, 7.5 and 10.0 per cent. Diffusion of monocaine was found to differ from that of procaine in the spinal fluid, and the level of sensory anesthesia sometimes continued to extend cephalad for as long as thirty minutes. "With the amounts used, 50 to 150 mg. in 5 per cent concentration in spinal fluid, the results observed during anesthesia and post-operatively indicate that complications are no more severe and of lower incidence than might be expected from procaine." In conclusion, they expressed the belief that monocaine is a safe, useful agent for spinal anesthesia when given in low concentration and in small or moderate doses.

LOCAL ANESTHESIA

Beutner and Calesnick²⁸ carried out experimental research to find the physiologic and chemical properties possessed by many of the widely used

local anesthetics. They concluded that efficient local anesthetic agents have so far been obtained only as ester compounds of benzoic acid, amino-benzoic acid or some related substituted benzoic acid (Nupercaine, quinolin carbonic acid, used in one instance). These acids are combined with some amino alcohol or a related compound (for Nupercaine, one having a diamino radical) that supplies the basic property. The ester-like loose combination between the acid and the amino alcohol is the essential indispensable characteristic.

Physiologically all efficient local anesthetics have been found to be convulsants and stimulants of the cerebral cortex, the convulsive power being approximately parallel with the efficiency of the local anesthetic agent.

Apparently it is more than a casual coincidence that all efficient local anesthetics are convulsants. They must possess a marked affinity to the nerve cells in order to depress selectively the terminal nerve fibers without injuring the cells.

Mousel,²⁹ Tuohy,³⁰ Adams³¹ and Seldon and Lundy^{32, 33} have recently published timely and worth-while papers covering the commoner regional nerve-block technics for all parts of the body. One finds a crystallization of valuable clinical experience in these writings that comes only after years of experience. These articles should be read by all anesthetists interested in the proper application of regional anesthesia in modern anesthesiology.

Much interest has been shown of late in the use of local infiltration and regional block anesthesia for obstetrics.³⁴⁻³⁷

SPINAL ANESTHESIA

Goldberg, Koster and Warshaw³⁸ write as follows:

By means of new chemical technics it is shown that procaine within the subarachnoid space remains essentially unchanged. The fall in concentration of procaine, which is responsible for the wearing off of spinal anesthesia, is due to vascular absorption. Once in the blood stream procaine is rapidly hydrolyzed (detoxified) by an enzyme. . . . At no time is there any appreciable trace of procaine in the blood; hence, the cause of various "toxic" effects which have been attributed to a procainemia must be sought elsewhere. . . . Nearly all the injected procaine (90 per cent on the average) is excreted in the urine, but only in the form of products of detoxication.

In a recent study of spinal anesthesia in normal, unoperated man, Smith, Rovenstine and their collaborators³⁹ have shown that anesthetic denervation does not produce renal hyperemia. Smith⁴⁰ has more recently reaffirmed this conclusion after a more complete review of the literature. In the first paper the authors suggested that the arteriolar

bed generally — apart from the skin — possesses considerably more autonomy than is usually attributed to it. They believe that blood pressure may change very little during high spinal anesthesia in normal, unoperated man. For the most part, such decrease as was observed in these unoperated patients was a result of the decrease in the stroke volume of the heart, which they attributed to a decrease in venous pressure.

The extreme falls in blood pressure observed during high spinal anesthesia are believed by Papper, Bradley and Rovenstine^{41, 42} to be the result of decreased venous pressure (and hence a decreased cardiac output) following opening of the abdomen and the attendant operative procedures inflicted in the face of vasomotor paralysis and loss of vasomotor defense. Trauma, hemorrhage, anoxia, the weight of metal and other items upon the abdomen, the pressure of packs between the viscera, the position of the patient, malaise, fever and other complicating factors may contribute to the progressive reduction in venous pressure and the ultimate embarrassment of the circulation.

There seems to be a trend toward wider clinical application of spinal anesthesia by anesthetists in general.⁴³ This appears to be due to increasing confidence in the ability of vasomotor drugs, plus intravenous fluids (saline and glucose solutions, plasma and blood) to combat the hypotension often associated with spinal anesthesia. In addition, certain refinements in technic for spinal anesthesia have given the anesthetist more control over the distribution of the drug in the subarachnoid space.^{44, 45}

Fractional (continuous) spinal anesthesia is gaining in favor and seems to have answered a real need where ensured relaxation is needed over long periods for difficult abdominal or orthopedic operations.⁴⁶⁻⁴⁹ To date there has been a lack of uniformity of opinion concerning the best anesthetic agent to use by this method.

SUPPORTIVE TREATMENT

Every effort should be made through the use of supportive treatment to prevent the onset of shock or to institute treatment before the condition has progressed irrevocably. Certain tests may detect shock during its earlier stages when significant changes are noted in the hematocrit, the specific gravity of the plasma and whole blood and the plasma protein level.⁵⁰ The benefit of whole blood and plasma transfusion to the patient in shock is beyond question. Elman⁵¹ has shown that a solution of hydrolyzed protein containing amino acids and polypeptides exerts a definite therapeutic effect, as evidenced by prolongation of the survival time, an increase in the amount of

hemorrhage that could be sustained and a higher level of blood pressure as compared with that in controls in whom dextrose alone was used or in whom there was no replacement.

Because of the part that tissue anoxia must play in the vicious cycle of shock, it is interesting to note the favorable effect of administering high oxygen concentrations reported in two recent papers.^{52, 53} Others⁵⁴ report that the course of events in hemorrhagic shock is in no way altered when venous anoxemia is prevented by administering oxygen at high pressure.

Beecher, McCarrell and Evans⁵⁵ have confirmed the observations of Seeley, Essex and Mann⁵⁶ that shock produced in dogs by exposure and manipulation of the intestine is slower to appear when barbiturate (sodium amytal) anesthesia is used than when ether anesthesia is employed. However, they found no significant delay in the onset of shock produced by hemorrhage when barbiturate anesthesia was used. Their observations together with those of Parsons and Phemister⁵⁷ and Blalock,⁵⁸ who found similar effects under barbiturate and ether anesthesia when shock was produced by muscle trauma, indicate that barbiturate as compared with ether anesthesia is not useful in delaying all types of shock.

Studies have been made by Seligman and Fine,^{59, 60} using a radioactive plasma protein, to test the prevailing opinion that an increased permeability of the capillaries exists in shock and that a subsequent loss of plasma into the tissues ensues, so that the effective circulating-blood volume falls to a level incompatible with life. They found that, whereas the integrity of the capillaries may be impaired in the latent shock phase, there is no evidence of the significant loss of plasma into the tissues in untreated fatal shock following hemorrhage.

Infusion of blood and other fluids through the bone marrow, as advocated by Tocantins,^{61, 62} gives another route by which large amounts may be administered. This method is particularly applicable in pediatrics, since transfusions to children under the age of two years are difficult to give by vein. It is also important in adult patients whose bodies are widely burned or whose veins are thrombosed. These intramedullary infusions are injected into the bone marrow of the manubrium sterni in adults and into the tibia or femur in infants. Doud and Tysell⁶³ were able to inject 9025 cc. of blood and 13,155 cc. of fluid into the sternal marrow of an adult by this method over a ten-day period.

COMPLICATIONS

The possibility that gangrene of a toe or finger will result from a nerve block with procaine

epinephrine solution is emphasized in all standard texts on regional anesthesia. The literature reports two such happenings, one involving a finger and the other a toe.^{64, 65}

At some time every surgical team will be called on to face the serious responsibility of a sudden cardiac arrest in the operating room. One such case, which occurred while the patient was receiving an inhalation anesthetic for a left lower lobectomy because of bronchiectasis, is reported in detail by Adams and Hand.⁶⁶ The probable cause of cardiac arrest, with treatment instituted that after twenty minutes resulted in a successful outcome, is given.

I was faced with a sudden cardiac arrest in a patient under spinal anesthesia during the last year. Approximately twenty-five minutes after the induction of anesthesia, while the surgeon was carrying out a high abdominal exploration, the pulse and blood pressure suddenly could not be obtained and respiration ceased. Vigorous artificial respiration carried on through an endotracheal tube with oxygen from a gas machine was started immediately, as was cardiac massage through the diaphragm, by the surgeon. One cubic centimeter of epinephrine was injected into the heart muscle, and the arrest was overcome in approximately three to four minutes after the pulse had disappeared. The patient made an uneventful recovery except for the loss of memory for a period of about two days.

Judging from the above experiences and those of Beck,⁶⁷ it seems reasonable to make every effort to save the lives of these patients. Prompt, adequate and properly selected methods of stimulating the return of cardiac function and the maintenance of adequate cerebral oxygenation are essential. Artificial respiration must be instituted with a gas machine after an intratracheal tube is inserted. Cardiac massage must be promptly started either through the chest or the left diaphragm. If the operation is not being carried on in the chest or abdomen, a transthoracic approach is quickly made. Small doses of epinephrine—0.5 to 1.0 cc.—injected into the cardiac muscle seem to be almost a necessity.

The surgical importance of atelectasis is obvious. It may complicate convalescence from any operation, and it is probably the most commonly encountered pulmonary complication after abdominal operation. Schmidt, Mousel and Harrington⁶⁸ present an interesting paper dealing with a series of 84 selected cases of postoperative atelectasis. Fifty-eight of the patients were men and 26 were women. The average age of both men and women was fifty years. There were no preoperative roentgenographic signs by which the likeli-

hood of postoperative atelectasis could have been foretold. In 52 of the cases the operations were on the biliary tract or stomach, in 9 cases on the colon, and in 8 cases on the kidney or its surrounding tissues; the number of cases representing other operations probably was not significant. In all cases in which atelectasis followed operation on the kidney, the lung affected was the one corresponding to the side on which the patient was lying. If treatment was begun within forty-eight hours after the complication occurred, the results were excellent. If the complication existed for seventy-two hours or longer before treatment was begun, recovery was usually slower, since secondary pneumonia had usually developed.

MILITARY ANESTHESIA

In an excellent article that brings the history of anesthesia in war surgery up to date since ether was discovered in 1842, Pender and Lundy⁶⁹ concluded with these predictions about anesthesia in the present war:

Chloroform will be the reserve anesthetic agent for use under adverse circumstances.

Ether will form the foundation anesthetic agent when other agents are not satisfactory.

Local anesthesia will be either used alone or supplemented whenever possible.

Nitrous oxide and oxygen will be most useful for simple induction and for short operations.

Spinal anesthesia administered by experienced hands will be safer than ever before for operations performed below the diaphragm.

Quick-acting barbiturates administered intravenously will be used more often than any other type of anesthetic agent.

Rectal anesthesia will be used seldom.

Cyclopropane will be unequaled for anesthetizing many patients in base hospitals.

The intratracheal method will be almost the routine manner of administration of the volatile anesthetic agent.

Martin⁷⁰ believes that the advances in anesthesiology since World War I are reflected in its inclusion in the organization of hospitals of the United States Army.⁷¹ Anesthesiology, for the first time, was set aside as a section by itself on the Surgical Service of the Tilton General Hospital, Fort Dix, New Jersey, for instruction of medical officers in the fundamental principles of anesthesiology.⁷²

Several anesthetists have related their experiences in England⁷³ and the Middle East⁷⁴ at large general hospitals. Much of the work was of the same general character as that seen in any large civilian hospital, except for the emphasis on traumatic cases. Inhalation anesthesia by the intratracheal route seems to have been most popular. Intravenous Pentothal Sodium was used widely for minor surgery, spinal anesthesia was seldom

used, and local anesthesia was used little if at all. Because the problems of anesthesia in a small portable hospital immediately behind the front lines are so entirely different from those encountered at a base hospital, inclusion in this article of part of a recent communication seems timely. Swinton,⁷⁵ commanding officer of a small portable hospital that functioned for months in New Guinea, writes as follows about anesthesia.

In about 500 operations that I saw performed practically in the front lines, Pentothal Sodium was used almost routinely. These boys come in tired out, dirty and already heavily narcotized at the aid stations. All of them are frightened, and most of them are in more or less shock. We use plasma by the gallon. Pentothal served 95 per cent of all purposes. Spinal anesthesia can be used in a few of the abdominal cases if the shock can be quickly and safely controlled, but I stuck to ether in these cases. It is hard work, though, when one is spoiled by the relaxation of spinal anesthesia. Pentothal is easy to carry, easy to prepare, not bulky, and almost foolproof in any operation requiring up to forty-five minutes to one hour. Most front line surgery can be done very rapidly and in less time than in civilian practice. No aftereffects and quick recovery so that evacuation is not interfered with are important points in this work. One patient in this group died, and Pentothal should never have been given to him—just plain stupid selection of an anesthetic agent.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

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CASE 29311

PRESENTATION OF CASE

First admission. A fifty-two year-old meat dealer entered the hospital because of abdominal distress and jaundice.

He was well until three weeks before admission when he developed attacks of severe abdominal and substernal distress after eating that lasted for several hours and were often associated with anorexia. At the same time a steady aching discomfort developed between the shoulder blades and persisted to the time of admission. During one attack of distress he vomited bile stained food without much relief. Nausea and anorexia developed and he became constipated. Four days prior to admission a physician told him that he was jaundiced and prescribed a bland fat-free diet, which relieved the epigastric distress and anorexia. The jaundice, however, deepened, the urine became dark, and the stools clay colored. There were no chills or fever. The patient denied the use of alcohol or drugs. During his illness he was said to have lost a great deal of weight.

The family and past histories were noncontributory.

Physical examination disclosed a well-developed, moderately jaundiced man in no apparent discomfort. The sclerae were deeply jaundiced. The heart and lungs were normal. There was a sense of fullness in the right upper quadrant of the abdomen but no masses were felt, and no tenderness or rigidity was elicited.

The blood pressure was 120 systolic, 70 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a hemoglobin of 128 gm and a white cell count of 7800, with 69 per cent neutrophils. The urine showed a + test for bile. A blood Hinton test was negative. The serum protein was 6.8 gm. per 100 cc., the phosphorus 3.3 mg., the phosphatase 170 Bodansky units and the bilirubin 3.9 mg. direct and 6.2 mg. indirect. The prothrombin time was 18 seconds (normal, 20 seconds). The stool was greenish brown and repeatedly guaiac negative.

*On leave of absence

A flat plate of the abdomen revealed a liver that was slightly smaller than normal. The spleen was at the upper limits of normal. No definite stones were seen. On the sixth hospital day an exploratory laparotomy was done, with a preoperative diagnosis of "obstructive jaundice, probably due to a stone in the common duct." At operation the gall bladder was moderately distended. There was no evidence of metastatic disease of the liver. The pancreas was about three times normal size, nodular and irregular. There was no evidence of fat necrosis. The common duct was about twice normal size and no stones were found. A cholecystgastrostomy was done. A pancreatic biopsy was reported as chronic pancreatitis with fibrosis.

Following operation the jaundice cleared, the urine became pale and the stools brown. Between the eleventh and eighteenth postoperative days he was given x-ray treatment (1200 r) over the pancreas. The patient was discharged on the twenty-fourth hospital day.

Second admission (fourteen months later) The patient re-entered the hospital because of the onset of dark urine, clay-colored stools and a nagging, sometimes painful sensation in the back between the shoulder blades. The patient had been fairly well and had been free from jaundice, bristling and malaise until one week prior to entry. Three days prior to entry jaundice appeared. There were no chills, fever, nausea or vomiting.

Physical examination was similar to that of the first admission. The liver edge was palpable two fingerbreadths below the right costal border.

The temperature, pulse and respirations were normal. Examination of the blood revealed a red-cell count of 5,250,000, with a hemoglobin of 15.1 gm, and a white-cell count of 8400, with 57 per cent neutrophils. The urine was normal. The serum bilirubin was 3.4 mg per 100 cc direct and 4.35 mg indirect. The stool was light tan, and guaiac negative. Gastric analysis failed to reveal free hydrochloric acid, either before or after a test meal. The stomach content was guaiac negative.

An x-ray film of the chest was negative. Because the patient desired to return home to consider operation, he was discharged, unimproved, on the seventh hospital day.

Final admission (six weeks later) After discharge he was awakened several times at night by mild epigastric discomfort that was partly relieved by warm water or milk. Four weeks prior to admission his stools became pale, and the urine dark brown. Three weeks prior to admission the jaundice deepened and generalized pruritus developed. His appetite decreased, but he had no nausea, vomiting, hematemesis or melena. Two

weeks prior to admission he developed diarrhea and often had two to seven movements a day for three or four days, but this was relieved by tincture of belladonna. The liver was felt 2 cm. below the costal margin in the right anterior axillary line, 6.5 cm. below in the midclavicular line, 8 cm. below the xiphoid, and 6 cm. below the left costal margin. The spleen was neither palpable nor percussable. There was no shifting dullness or fluid wave.

The temperature, pulse and respirations were normal.

The urine showed a + test for albumin, a ++++ test for bile and no urobilinogen. The serum bilirubin was 10.4 mg. per 100 cc. direct and 14.8 mg. indirect. Five days later it was 12.3 mg. direct and 17.5 mg. indirect. The prothrombin time was 23 seconds (normal, 18 seconds). The stool was gray, guaiac negative and contained neutral fat.

The jaundice increased, and the patient complained of increased urinary frequency and vague abdominal discomfort. After preparation with saline-glucose infusions and water-soluble vitamin K, an exploratory laparotomy was performed on the eleventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. ROBERT R. LINTON: The history of the first admission without any question indicates that we are dealing with a patient with obstructive jaundice. There are a number of conditions that can produce obstructive jaundice, the commonest of which, of course, is cholelithiasis with a stone in the common duct or an extrahepatic lesion producing pressure on the common duct, such as carcinoma of the head of the pancreas or carcinoma of the papilla of Vater. Carcinoma of the biliary passages can also produce obstructive jaundice, but it is my opinion that this lesion produces obstructive jaundice of complete degree and of a much more rapid nature than this man developed. Another cause of jaundice that one ought to consider is cirrhosis of the liver. This is usually not complete obstruction, however, and associated with it, one usually finds a large spleen. We have evidence here by x-ray and physical examination that the spleen was relatively small or normal in size. Another condition that one encounters is pancreatitis, which sometimes produces a sclerosing type of lesion that obstructs the common duct as it passes behind the duodenum.

I do not believe there is anything in the laboratory findings of diagnostic importance. It is interesting that the phosphatase was elevated, which is the usual finding in obstructive jaundice. The

bilirubin was elevated but not markedly, 3.9 mg per 100 cc. direct, with a total of 6.2 mg., which indicates that the patient had obstructive jaundice rather than jaundice due to blood destruction. The prothrombin time was essentially normal, so that he did not have a hemorrhagic diathesis.

At the operation we learn that the gall bladder was moderately distended; no stones were found, and the pancreas was enlarged. These observations confirm Courvoisier's law, namely, that a dilated gall bladder in the presence of jaundice usually means extrahepatic biliary obstruction rather than obstruction due to stone. It is of interest that a biopsy of the head of the pancreas was reported "chronic pancreatitis with fibrosis." Biopsies of the head of the pancreas are, I believe, notoriously inaccurate because of the fact that in carcinoma of the pancreas one may have obstruction of the pancreatic duct with a good deal of thickening and fibrosis of the pancreas, and what one thinks is a malignant lesion is really secondary fibrosis from obstruction of the pancreatic duct by carcinoma. So far as the story at the first admission is concerned one must decide whether one is dealing with carcinoma of the head of the pancreas or pancreatitis due to unknown causes, both of which produce obstructive jaundice. The fact that the patient received 1200 r of x-ray therapy makes me inclined to think that at that time the diagnosis of cancer of the pancreas was favored over that of pancreatitis.

At the second admission, fourteen months later, the patient re-entered because of the onset of dark urine, clay-colored stools and a painful sensation between the shoulder blades. He had been relieved temporarily by the cholecystgastrostomy, which apparently functioned very well for a little over a year, when his symptoms began to return.

After a period of six weeks from the time of the second admission the patient returned with evidence of marked obstructive jaundice, which had resulted in a large liver. It is interesting that he developed diarrhea of from two to seven movements a day for three or four days. If he had pancreatic obstruction, I am surprised that that came on so late. If he had had pancreatic-duct obstruction without any external pancreatic secretion going into the intestinal tract, I should have thought that he would have had steatorrhea earlier. His condition was getting worse, as indicated by the serum bilirubin, which jumped from a total of 14.8 to 17.5 mg. in five days' observation. I believe the diagnosis still lies between cancer of the head of the pancreas and chronic pancreatitis.

In favor of its being carcinoma of the head of the pancreas is the fact that this is the commonest

lesion that produces obstructive jaundice in cases in which the pancreas is involved. I have seen one patient* who had had cholecystgastrostomy who lived for three years before he finally died of carcinoma of the pancreas; we wondered, until we finally did ascertain what his trouble was at autopsy, whether we were not dealing with chronic pancreatitis. The case we are discussing did not go quite that long, only fourteen months. Another interesting point is, Why did this man do so well for over a year and then develop obstructive jaundice? Certainly the cholecystgastrostomy worked well at first, and why it did not continue to work well seems a little strange. The fact that it did not work continuously and relieve the jaundice permanently suggests that one was dealing with a malignant lesion and that the malignant disease had eventually involved the cholecystgastrostomy. We have no evidence, however, so far as physical examination goes, that the patient had metastatic disease involving the abdominal cavity, such as a nodular liver or other masses.

On the other hand if one assumes this is pancreatitis, then one has to postulate that for some reason or other the cholecystgastrostomy failed to function after a period of time. I think we have observed on occasions that cholecystgastrostomies and choledochostomies do close off spontaneously if the normal biliary circulation through the ampulla of Vater is re-established, and I think that is a possibility in this case. If so, it would favor the diagnosis of pancreatitis. It seems to me on the evidence presented here, however, that the more likely diagnosis is carcinoma of the pancreas with extension and finally obstruction of the short-circuiting operation that was performed.

DR. BENJAMIN CASTLEMAN: Dr. Allen, will you tell us your impression of the case?

DR. ARTHUR W. ALLEN: Dr. Jones and Dr. Benedict are both interested in this patient. Dr. Linton's reasoning about the first admission was I think in accordance with our own. We thought it was possible that, with the biopsy of the pancreas, we did not obtain a piece of the true lesion, although Dr. Mallory made sections of it and felt quite certain that it was an inflammatory process. Dr. Jones has just reminded me that the process involved the entire pancreas and was not localized to the head, as we nearly always see it in cases of carcinoma of the pancreas with jaundice.

Dr. Linton wondered why the patient had radiation afterward and thought that might help him in his diagnosis of malignant disease. The reason he had that treatment was based on the idea of

Morton,* of Rochester, New York, who has suggested that, since the pancreas is so much like the parotid gland in its structure and since radiation works so well in acute parotitis, mild radiation in pancreatitis may be of value. So we gave a small amount of x-ray therapy, 1200 r, divided in four doses. He recovered so completely that we believed that he really did have an inflammatory rather than a malignant lesion. Dr. Jones and I even considered the possibility of disconnecting the cholecystgastrostomy for fear of an ascending cholangitis. When the patient came in to Dr. Jones for a check-up six months later, he found evidence of a good deal of liver damage, which he will tell you about, and the question of reoperation was dropped, until he became jaundiced again and began to have symptoms. We reasoned very much as Dr. Linton did; that is, we might have made a mistake in our original diagnosis and the patient might have had a respite from carcinoma during this period. Dr. Benedict therefore performed a peritoneoscopy and found a swollen liver without any nodules; a biopsy showed obstructive jaundice.

We then explored the patient, after adequate preparation. He had 100 per cent dye retention in the liver. At operation, we found a small, hard pancreas, which was possibly one fourth the size that it was originally, and another biopsy specimen, a generous one, examined by Dr. Castleman showed fibrosis of all the pancreatic elements with nothing but islet cells left in the gland. We therefore reasoned that he had had inflammatory disease from the start and that the reason the cholecystgastrostomy had closed was exactly as Dr. Linton suggested—during a period of his early convalescence the portion of the duct that went through the pancreas was released, the duct functioned again and therefore nature had closed the artificial opening. We further reasoned that, at this time, a permanent arrangement for the passage of bile into the intestine should be made. We therefore anastomosed the cut end of the jejunum to the fundus of the gall bladder in an isoperistaltic direction, re-anastomosing the other end of the jejunum to the side of the gut after the method of Roux. The procedure was well planned and there were no difficulties, but, as Dr. Castleman will tell you, it was too much for a man who was as sick as this one. The patient died two days later with what we believed to be liver failure, quite like the kind of death we used to see in patients who had their hepatic arteries tied accidentally.

*Morton, J. J., and Widmer, S. Diagnosis and treatment of acute pancreatitis. *Ann. Surg.* 111 851 #63, 1940

DR. CHESTER M. JONES: There are one or two other points of interest. I saw this patient a year after the first operation and followed him closely. He had no symptoms except diarrhea. He recovered from his jaundice, about a month after the first operation there being no trace of it. At that time the liver was two fingerbreadths below the costal margin. In other words it had diminished in size appreciably. Six months after operation he was feeling better and had no jaundice, the liver was just barely palpable, the bilirubin was 0.4 mg. per 100 cc., a perfectly normal figure, and the dye retention was 10 per cent. That made me wonder whether he had some permanent liver damage.

Six months later he had no jaundice, but the liver was two fingerbreadths below the costal margin, definitely larger. Because of the discrepancy we checked the laboratory findings and found that he had 60-per-cent dye retention and increased blood bilirubin. He remained free of jaundice until three or four weeks before he finally was operated on, and then, rather suddenly, clinical jaundice recurred. At that time the dye retention was 100 per cent. Dr. Allen and I thought that regardless of the cause of the block there must have been a lot of liver damage, which was explainable on the basis either of diffuse hepatic involvement by carcinoma, which was unlikely, or a diffuse process in the nature of a biliary cirrhosis. The biopsy specimen that Dr. Benedict took had the microscopic appearance of biliary cirrhosis. In other words, the biopsy fitted the clinical picture, but it was still impossible to tell what was the underlying cause.

DR. LINTON: I still do not see why the patient became jaundiced so suddenly at the end.

DR. JONES: I think what happened was that he had a fairly active low-grade inflammatory process involving the pancreas and probably the liver itself. At any rate at a point in the course of the illness the cholecystgastrostomy closed over completely. When Dr. Allen operated he could not get a probe into the opening of the gastrostomy. Is that not correct, Dr. Allen?

DR. ALLEN: Yes; there was no opening into the stomach.

CLINICAL DIAGNOSIS

Obstructive jaundice.

DR. LINTON'S DIAGNOSIS

Carcinoma of the pancreas?
Chronic pancreatitis?

ANATOMICAL DIAGNOSES

Chronic pancreatitis, severe, with stenosis of common bile duct.
Obstructive biliary cirrhosis of liver.
Cholelithiasis.
Choledocholithiasis.
Ascites.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The biopsy showed that the pancreas was, as had been described at the second operation, very small and fibrotic. The sections from the autopsy material confirmed the biopsy sections, showing a diffuse interacinar and perhaps interlobular type of chronic fibrous pancreatitis. There was atrophy of the acinar cells and replacement of much of the parenchyma by fibrosis and lymphocytic infiltration so that only the islet cells and ducts remained. This was much severer in the region of the head of the pancreas but was also present throughout the organ. The opening of the bile duct at the ampulla was tiny, and the common bile duct above was markedly dilated, about 3 cm. in circumference. This stenosis had undoubtedly been produced by the surrounding fibrous pancreatitis. There was no carcinoma. In the common duct, as well as in the gall bladder, we found muddy material and a few small stones (0.5 to 1 mm. in diameter), which was evidence that the infection was still going on in the biliary tract.

The liver showed widespread fibrosis of the biliary type, with proliferation of the bile ducts characteristic of fairly long-standing obstructive jaundice. There were 2 liters of bile-stained fluid in the abdominal cavity. The anastomoses were intact, and I believe that death was due to liver failure. I find it hard to conceive that the bile duct was ever patent enough to allow for a closure of the anastomosis because of disuse. I think he was getting all his bile through the anastomosis until it closed. Why, I do not know.

DR. ALLEN: My reasoning about it is that at the time of the first operation the pancreas was tremendously swollen, four times the normal size, from the inflammatory process, that the edema around the pancreatic portion of the duct produced the jaundice and then when the anastomosis was established the inflammation in the pancreas receded enough afterward to allow a temporary passageway for the bile to go through its natural course. During the temporary normal passageway, the anastomosis shut down. The duct did not completely close off—again due to the fibrosis—until one of these 1-mm. stones got down into

the narrow channel. That probably explains the question Dr. Linton asked about the suddenness of the final jaundice. As a matter of fact it took two or three weeks for it to become complete.

DR. CASTLEMAN: I do not believe that the bile duct would open when the pancreas became scarred; in fact this might tend to close it more completely.

DR. ALLEN: We have had many cases of jaundice associated with pancreatitis that have completely cleared up. I have seen only one previous case of complete fibrosis of the pancreatic portion of the bile duct. It may happen quite frequently, but that is the only other one I have seen. In that patient the pancreatitis was secondary to a penetrating duodenal ulcer.

DR. CASTLEMAN: This is the first true case of widespread chronic pancreatitis that I have ever seen. Mild degrees of focal chronic pancreatitis are not uncommon autopsy findings, but this severe form is distinctly unusual.

DR. LINTON: The original obstruction could have been due to edema. Fibrosis would take months.

DR. ALLEN: Yes; "edema" is the word for the early episode, and "fibrosis" for the final one.

DR. JONES: Furthermore, the patient had a slight amount of bile going through until the day of operation. X-ray films taken three weeks before failed to show barium going into the gall bladder, which it will do if the stoma is patent.

DR. ALLEN: That is correct. At the second admission roentgenograms showed no passage of barium from the stomach to the gall bladder.

DR. JONES: Dr. Allen and I discussed this case after operation. If we were confronted with a situation like this, where the liver was badly damaged, it would be worth considering a two-stage operation, simply relieving the block for the moment with drainage and doing the complete operation later. This is all in retrospect, but I think it should be mentioned.

DR. ALLEN: I have disliked doing two-stage operations for this type of obstructive jaundice because we rarely succeed in getting to the second stage. Sudden decompression of the liver has caused the patient to continue his decline. Possibly we should have been smart enough to have thought of operation when the dye retention rose to 60 per cent. We may never see another patient like this. It is an unusual case.

DR. LINTON: I wonder why you did not do the Roux type of operation rather than cholecystgastrostomy at the first operation.

DR. ALLEN: I expected this to be a temporary affair, and planned to disconnect it after the patient had recovered from the pancreatitis. I did not suppose he would develop fibrosis.

CASE 29312

PRESENTATION OF CASE

First admission. A seventy-nine-year-old Italian laborer entered the hospital because of a chronic ulcer of the right elbow occurring in the scar of an old burn.

Approximately forty years prior to admission the patient burned both elbows severely. These healed slowly with a great deal of scarring but without limitation of joint motion. Approximately one year prior to admission the scar about the right elbow ulcerated, often bled a great deal and never completely healed despite local treatment.

The family and past histories were noncontributory.

Physical examination disclosed a fairly well-preserved old man who seemed apprehensive. The heart, lungs and abdomen were normal. On the dorsal aspect of the left elbow over an area approximately 5 by 4 cm., involving the lower end of the upper arm and an equal area of the lower arm, were irregular scars traversed with many firm crusted ridges. The involved area of the right elbow measured approximately 14 by 12 cm. and was almost symmetrical in position to that of the left arm. In the center was a shallow ulcer, 12 by 8 cm., covered by shreds of necrotic tissue, fresh blood and greenish-yellow purulent exudate. There was almost no granulation tissue.

The blood pressure was 148 systolic, 90 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a red cell count of 4,440,000, with a hemoglobin of 84 per cent, and a white-cell count of 8200. The urine was normal. A blood Hinton test was negative.

X-ray films of the right elbow showed a large area of bone destruction from the upper one-third of the shaft of the ulna with some soft-tissue swelling. There was no evidence of new-bone formation. There was a pathologic fracture through the area of destruction. A chest roentgenogram showed clear lung fields. There were several old fractured ribs on the right side. Following a report of epidermoid carcinoma, Grade 2, on a biopsy specimen from the edge of the ulcer of the right elbow, the right arm was amputated at the junction of the middle and lower thirds of the humerus. Dissection of the amputated limb showed extension of the neoplastic tissue from the base of the tumor into the subjacent proximal end of the ulna, with pathologic fracture 4 cm. from the proximal articular surface. Because of the severe local infections, the patient received a preoperative course of sulfadiazine. He was discharged on the eighteenth hospital day.

DR. CHESTER M. JONES: There are one or two other points of interest. I saw this patient a year after the first operation and followed him closely. He had no symptoms except diarrhea. He recovered from his jaundice, about a month after the first operation there being no trace of it. At that time the liver was two fingerbreadths below the costal margin. In other words it had diminished in size appreciably. Six months after operation he was feeling better and had no jaundice, the liver was just barely palpable, the bilirubin was 0.4 mg. per 100 cc., a perfectly normal figure, and the dye retention was 10 per cent. That made me wonder whether he had some permanent liver damage.

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Final admission (one year later). The patient re-entered because of fever, foul breath and pain in the right chest.

Following discharge the patient was well until four months prior to admission, when he developed a "cold," characterized by cough, fever, chills, sweating and a sharp pain in the left lower chest anteriorly. After three and a half weeks in his community hospital he apparently made a satisfactory recovery, and an x-ray film of the chest prior to discharge was said to have been negative except for "congestion." Three months before entry he had a tooth extracted under local anesthesia.

Approximately six weeks before entry he again developed a cough and complained of a sharp pain across the epigastrium and in the precordial area on coughing. He soon became extremely weak, lost his appetite and went to bed. Three days prior to admission he suddenly coughed up a large amount of bloody, foul-smelling material, and since then he had continued to bring up fairly large quantities of foul-smelling sputum, without blood. During the three days prior to admission he had several chills, with fever as high as 101°F.

Physical examination disclosed an emaciated man with a great deal of respiratory distress. The chest was large, and there was dullness to flatness with diminished breath sounds and coarse moist rales over the posterior right chest below the scapula. In the right axilla a loud "leathery" creaking sound was audible on both inspiration and expiration. There was no diaphragmatic excursion on this side. A blowing systolic murmur was audible over the entire precordium, best heard at the apex. Abdominal examination was negative. The right upper arm stump was well healed, and the scar about the left elbow had not changed since the previous examinations. There was no clubbing of the fingers.

The blood pressure was 115 systolic, 55 diastolic. The temperature was 100°F., and the pulse and respirations were normal.

A chest roentgenogram demonstrated a large abscess above the right diaphragm posteriorly, which was 7.5 cm. across at the fluid level. The abscess wall was rather thick and irregular, and the outlines not sharply defined. No definite tumor mass was seen in the hilar area.

Examination of the blood revealed a red-cell count of 3,800,000, with a hemoglobin of 13 gm., and a white-cell count of 16,000, with 82 per cent neutrophils. The urine was acid and had a specific gravity of 1.020; the sediment contained innumerable red cells, 4 to 6 white cells and several granular casts per high-power field. The sputum

was tenacious, foul smelling, and yellow green, with rusty streaks. Bronchoscopy showed no widening, deviation or fixation of the carina. The right upper and middle lobe orifices were normal. The mucosa throughout the right main and lower lobe bronchi was markedly reddened and somewhat edematous and contained a considerable amount of a brownish-red, thin secretion. This appeared to be coming from the lower lobe bronchus, but its exact origin could not be determined. The mucosa was smooth, and there was no intrinsic mass or evidence of extrinsic pressure.

The patient continued to run a fever ranging between 100 and 102°F. Postural drainage was ineffectual, and on the thirteenth day a first-stage drainage of lung abscess was performed. A chest roentgenogram the next day showed no change in the abscess cavity. In addition there was an area of consolidation in the left mid-lung field. Four days later the second stage was done. The patient died soon after operation.

DIFFERENTIAL DIAGNOSIS

DR. RALPH ADAMS*: The assumption that chronic irritation was an etiologic factor in the production of this cancer from a burn scar seems to be admissible without argument. The carcinogenic role of continuing low-grade injuries to tissues by infection and by mechanical, thermal and chemical irritants has been well established and is generally accepted. Taylor, Nathanson and Shaw¹ reviewed 430 cases of carcinoma of the extremities and found definite precancerous lesions to exist in 196 cases. Eleven cancers occurred in the sinuses of chronic osteomyelitis, 13 in varicose ulcers, and 23 in the scars of old burns. The 11 cases of cancer found in osteomyelitis sinuses all had appeared in lesions more than fifteen years old. I know of no case in which cancer has appeared in a chronic varicose ulcer in a shorter period. There is in the literature no report of carcinoma appearing primarily in an empyema sinus, but I have one unpublished case in which epidermoid carcinoma developed in a chronic empyema sinus twenty-six years after its onset. However, highly malignant cancer has been observed in scars of old burns within two years. The point being made is that an ulcer appearing in an old burn scar more than fifteen years after the original injury is almost surely malignant and should be treated as such immediately.

This hospital had no opportunity to offer treatment until the cancer had advanced to bone destruction and carried out the appropriate therapy—amputation. Metastatic disease in the chest, the commonest site of carcinomatous metastases

*Surgeon, Lahey Clinic.

from the upper extremity, was properly excluded so far as possible by negative chest roentgenograms preoperatively.

Within eight months, however, the patient developed signs of lung and pleural involvement and received clinical relief of symptoms by rest in his local hospital; however, x-ray signs of "congestion" persisted, indicating that he had more serious disease than a "cold" or congestion or simple bronchopneumonia. A week after leaving the local hospital and three months before coming here he had a tooth extraction under local anesthesia. Six weeks thereafter and six weeks before entry here, he again developed signs of pneumonitis with infection, and three days before entry a diagnosis of putrid lung abscess was made, which was self-evident when he coughed up foul, bloody pus.

The record is not clear on this detail but I dare say that the patient was never entirely free from cough and a sensation of something wrong in his chest from the original chest episode four months prior to entry until his eventual admission, for the following reasons. In the first place, six weeks is an unusually long interim between a tooth extraction and the appearance of a lung abscess if such is developing. An additional five weeks, for a total of eleven, is in my experience unique between the onset of suppurative pneumonitis and the production of foul sputum. Secondly, according to statistics, a patient with this diagnostic and symptomatic background should have malignant disease in his chest. Thirdly, although the record does not mention it, the first chest x-ray film at the time of the second admission shows distinct erosion of the left fifth rib and adjacent translucence in the peripheral lung field, as well as the described abscess in the opposite lung. Fourthly, the walls of the abscess are much denser and thicker and more irregular than one is accustomed to see in putrid lung abscess but are characteristic of abscess secondary to malignant degeneration. And, finally,—and I shall ask the X-ray Department for confirmation or rebuttal in a moment,—it is my impression that the chest x-ray film taken one day after the first-stage drainage of the right lung abscess, and twelve days after the previous film, reveals marked destruction of the left fifth rib and pathologic fracture in addition to the area of consolidation in the left mid-lung field cited by the case abstract as having just appeared. A few years ago the statement was frequently made that metastatic pulmonary lesions do not cause hemoptysis, but since then a few exceptions have been encountered,² and we have to abandon the rule as a statement of invariable fact; it is, however, a good

generalization. Similarly, I have one proved example that metastatic malignancy can suppurate to produce bloody and foul sputum, and I believe that this case furnishes a second example. The bronchoscopic findings are consistent with that theory. The point whether the abscess is pyogenic or cancerous is an academic one, but it is a feature of the case that requires discussion.

Before making a final diagnosis may I have a first-hand interpretation of the films from the X-ray Department?

DR. BENJAMIN CASTLEMAN: The following statement appears in the x-ray report, "The posterior portion of the left fifth rib cannot be traced as it crosses the area of involvement. I believe the patient should have a film of the rib." Apparently that film was never taken.

DR. MILFORD SCHULZ: It is quite obvious that the posterior portion of the left fifth rib is involved. Certainly the short interval of time suggests that the rib must have been involved in the earlier film. Yes, it is; here is an area of destruction in the same place—apparently a fracture occurred in the meantime.

DR. ADAMS: In my halting clinical way I hesitated to arrive at a diagnosis of the rib lesion and took the liberty to ask Dr. Hugh Hare, a radiologist, to check that finding, which he did.

In conclusion, I shall state my diagnosis as carcinoma in an old burn scar of the right arm, with chest-wall and pulmonary metastases and putrid lung abscess.

DR. HELEN PITTMAN: When I saw this man,—I acknowledge that I missed the lesion in the rib,—he obviously had a stinking lung abscess. I cast my vote in favor of its being distal to an intra-bronchial metastasis, going on the same reasoning as Dr. Adams has used.

CLINICAL DIAGNOSES

Lung abscess, right lower lobe.
Carcinoma of lung (? primary or metastatic), right lower lobe (?).
(Carcinoma of right arm.)
Amputation of right arm.

DR. ADAMS'S DIAGNOSES

(Epidermoid carcinoma, in scar of burn of right arm.)
Metastatic epidermoid carcinoma of lungs, with secondary suppuration, and of ribs.

ANATOMICAL DIAGNOSES

(Epidermoid carcinoma in scar of burn of right arm.)
Metastatic epidermoid carcinoma of lung, right lower lobe, with secondary suppuration.

Metastatic epidermoid carcinoma of ribs and liver.
Pulmonary abscesses, left upper lobe.
Empyema, bilateral.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The second-stage drainage of the large abscess was done, and at that time a biopsy of the wall of the abscess was made. The diagnosis was epidermoid carcinoma. The patient died the day following the drainage.

At autopsy there was empyema on both sides. The abscess had been unroofed and was lined with shaggy gray-green granular tissue. Although grossly it looked like an ordinary lung abscess, epidermoid carcinoma was found in its wall microscopically. In other words, all but a rim of tumor had become necrotic. This was not an abscess distal to a tumor but one within the tumor. In the left upper lobe there were two abscesses that in gross looked very much like the one in the right lower lobe, but sections of both these abscesses showed no evidence of carcinoma. They appear to have been secondary lung abscesses, probably from the infected tumor. Unfortunately no section of the rib was made, but there is no

doubt that it would have proved to be metastatic epidermoid carcinoma. A section of the liver also showed metastatic tumor.

When I first saw the biopsy specimen of the right lower lobe I was doubtful whether it was a primary carcinoma of the lung or a metastasis from the carcinoma of the arm. The former is still a possibility, but the peripheral location of the lesion and the similarity of the histologic appearance of the two cancers make metastatic carcinoma more likely. The bone and liver metastases could come from either primary tumor.

DR. FLETCHER H. COLBY: Did you find the source of the blood in the urine?

DR. CASTLEMAN: No. There were a few changes in the tubules that suggested degeneration, perhaps due to drug therapy, but I hesitate to say much about it because the autopsy was done sixteen hours after death, when one usually finds post-mortem tubular degeneration.

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PROCUREMENT AND ASSIGNMENT OF NURSES

LAST week the War Manpower Commission announced that its subdivision in charge of nurse procurement and assignment, the Nursing Supply and Distribution Unit, had been made an integral part of the Procurement and Assignment Service. The Nursing Division will be supervised by the Directing Board, of which Dr. Frank H. Lahey is chairman, and as with the divisions covering physicians, dentists, sanitary engineers and veterinarians, the latter is charged not only with recruitment of sufficient nurses to meet the needs of the armed

forces but also with minimum adequate nursing care for nonmilitary governmental agencies, the civilian population and industry.

Two nurses, Miss Katherine Tucker, of Philadelphia, and Miss Laura Grant, of New Haven, Connecticut, have been appointed to the Directing Board, and the latter will be assisted by the Nursing Advisory Committee, in addition to newly appointed representatives on the already existing advisory committees that are concerned with problems affecting nurses. The work at the Washington office will be under the direction of Miss L. Louise Baker, an assistant executive officer of the Procurement and Assignment Service, assisted by Miss Ruth A. Heintzelman.

The field activities of the Nursing Division will be carried out by state and local committees. At the former level, the Supply and Distribution Committee of the Nursing Council for War Service, which represents the various nursing organizations in each state, will act as the State Committee for Nurses of the Procurement and Assignment Service; whereas local matters will be handled by the nursing councils in each community. Both the state and the local committees will function independently of but in co-operation with the corresponding committees having to do with the procurement and assignment of physicians.

Because of all this it seems likely that many of the present-day problems dealing with nurses will be handled more expeditiously and more efficiently than they have been in the past.

ARNOLD CARL KLEBS*

THE death of Arnold Carl Klebs, a distinguished American physician, in Nyon, Switzerland, on March 6, 1943, brings to a close a life of unusual achievement in medicine and medical bibliography. Known to comparatively few physicians of the present generation in America, his influence, nevertheless, was widespread among a small group of doctors particularly interested in medical history.

*An exhibit of books, pamphlets and pictures having to do with Dr. Klebs is now on display in the rotunda of the Boston Medical Library.

As a specialist, moreover, he was a leading figure in this country at the turn of the century in the fight against the "great white plague." In later years his work as the bibliographer of the scientific and medical incunabula was deeply appreciated in scholarly circles. Klebs, like his predecessor, Conrad Gesner, kept his home open in Switzerland to a host of American visitors who found his delightful villa at Nyon, on the shore of Lake Geneva, a welcome resting place in their peregrinations about Europe. Many a weary doctor, exhausted from a great international congress, sought relaxation in this quiet retreat. One found, moreover, an energetic and active man ready to exchange ideas in a stimulating and brilliant manner, often prodding his friends to bring out the best that was in them, and at the same time adding to the conversation, based on a wealth of experience, a keen summary from his own mind. Klebs was, moreover, an ardent correspondent with physicians both in Europe and America. In modern times he must have had few equals, and his pungent, philosophic letters are now the treasured possessions of many who kept this literary and scientific bond throughout the passing years.

Son of Edwin Klebs,¹ an early student of pathology and the co-discoverer with Loeffler of the diphtheria bacillus, Klebs was born in Berne, Switzerland, on March 17, 1870. His early years were peripatetic for, before he received his medical degree at Basel in 1895, his father had held successive chairs in the universities at Berne, Würzburg, Prague, Zurich and Karlsruhe. Klebs became well grounded in the classics and spoke and read with equal facility German, French, Italian and English. One can hardly conceive of a training wider in scope, and as the years went by, he always stood out as an internationalist of the first degree. Because of his facility in languages, he could easily and quickly grasp facts and ideas difficult for many because of language deficiencies. His keen mind, moreover, seemed to miss little.

After receiving his medical degree² in 1895, Klebs served as an instructor in pathology in Zurich, spent a summer as locum tenens at Vitznau and carried on some postgraduate studies at London and Paris. It was this thoroughly trained and brilliant student who came to America with his father in 1895. The elder Klebs first settled in Asheville, North Carolina, where he conducted laboratory and clinical investigation in a private tuberculosis sanatorium. Within a year, however, he was called to the chair of pathology at Rush Medical College in Chicago, a position that he held until 1900, when he returned to Europe. Before he left, his son, who in 1898 married Margaret Forbes, daughter of J. Malcolm Forbes, of Milton, Massachusetts, went to Chicago to practice, after having acted as head of a tuberculosis sanatorium in Citronelle, Alabama. He became a citizen of the United States in 1904 and remained in Chicago until 1909. During this period his main interests were in tuberculosis, and he soon became a recognized leader in the field. As director of the Chicago Tuberculosis Institute he was an ardent advocate of the open-air treatment, then an innovation, and he energetically supported the early work of Trudeau and others. Klebs's forceful personality was soon recognized by Billings, Musser, Jacobs, Osler and other students of tuberculosis throughout America. He worked hard, reading papers in various parts of the country, and finally culminated his endeavors in the editorship of a volume by American authors entitled *Tuberculosis*,³ published in 1909. As a background for this book he collected over three thousands reprints of articles on tuberculosis. These he carefully analyzed and published as a bibliography appended to the work. For authors he sought the best in the field, and contributions were forthcoming from Baldwin, Brown and Trudeau, of Saranac, Biggs, of New York, Coleman, of Augusta, Georgia, Minor, of Asheville, North Carolina, and Webb, of Colorado Springs. Unusually clear Roentgen plates for the time were furnished by Cole, of New York.

This volume was the best summary in English of the subject in 1909 and still may be read with profit. Klebs kept his interest in tuberculosis after 1909, although he did not take an active part in the campaign against it except on rare occasions. At the Fifteenth International Congress on Hygiene and Demography, held at Washington in September, 1912, he served as vice-president of the Section on the Control of Infectious Diseases.

Before his retirement in 1909, Klebs had married for a second time, his first wife having died in 1899. He went to Switzerland to live, first at Ouchy-Lausanne, and later at Nyon. Although making his home abroad, Klebs made frequent visits to the United States, and indeed lived in Washington during the period of World War I and in New York City subsequently for extended periods. Although he never forgot his adopted country, his heart was in his native Switzerland, and there at Nyon he established his library, using a small building on the grounds of his villa for this purpose. This two-story structure was literally lined with books and it became a true workshop of an intense, ardent spirit who exhibited, as few others have done, Osler's master word in medicine, "work." In this building, so delightfully situated, he deposited his father's books on pathology and allied subjects and assembled the apparatus necessary for his historical research.[†] Whatever he did, he did thoroughly, and each paper that came from his pen in later years was the result of many hours and even years of carefully planned research.

Klebs' first historical investigation concerned variolation, stemming from his father's interest in the subject. To his review of the subject,⁴ read before the Johns Hopkins Hospital Historical Club in 1912, he characteristically added a bibliography of six hundred items, and followed this with a paper in German on the same topic in 1914. This work brought him in contact with early American medicine: Zabdiel Boylston, Cotton Mather, New England and the Indians, subjects

which continued to interest him throughout his life.

His next major work related to Leonardo da Vinci. He read a paper on da Vinci's anatomical studies⁵ before the Society of Medical History of Chicago in 1915, at the same time, no doubt, renewing his old friendships in that city. He was living in Washington at the time, working in the Army Medical Library, and had already started his studies on incunabula, using the collection in that library as the basis for his fundamental researches in this field. He began by cataloguing those at hand, and soon contributed some sound ideas regarding classification of incunabula in general.⁶ Klebs's scheme was widely adopted by librarians and cleared up many points in descriptive labeling. He was soon led to the fifteenth-century herbals, books scarcely recognized at the time as a distinctive group, and he compiled an extensive catalogue. He⁷ later wrote that he had "travelled thousands of miles to visit libraries, to consult numerous catalogues, had an endless correspondence, hundreds of photographs, only to complete and later to correct the data of my list." A similar list of plague tracts⁸ was made, followed by more extensive investigations with Sudhoff,⁹ published in 1926. These authoritative listings have now become the standard references to the subjects and testify to Klebs's sound scholarship in both their completeness and accuracy.

Various papers on incunabula, appearing from 1926 to 1938, culminated in his classic short-title list of scientific and medical fifteenth-century books,¹⁰ a book constantly referred to by medical bibliographers throughout the world. It was to have been an introduction to a more extensive study, for Klebs had collected photographs and complete descriptions of over three thousand incunabula of medical or scientific interest, and this material lay in his library, ready to be brought to light, at the time of his death. Superbly ordered, it only awaits the final touches of some future scholar. The short-title list, however, is a royal monument to a man whose life was de-

[†]Dr. Klebs's library will eventually be transferred to the Historical Library of Yale University School of Medicine, where it will be added to the Cushing-Fulson Collection.

voted to sound bibliographic research, and because of it, all scholars are grateful.

Some estimate of the affection and esteem with which Klebs was regarded can be gained from the number of papers published in his honor on his seventieth birthday in 1940. Because of the war most of his European friends were unable to contribute to a birthday volume; however, the Institute for the History of Medicine at Johns Hopkins University issued a large, special number of its bulletin containing papers by his friends and associates.¹¹ Never a teacher or head of an institute, he had no pupils in the usual sense of the word; but his influence was widespread, and he inspired a group of contemporaries to expand the cultural side of medicine by his writings and by the impact of his forceful personality. In America, his adopted country, he left an enduring stamp on humanistic studies and on the history of medicine.

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MEDICAL EPONYM

ADIE SYNDROME

This was discussed by William John Adie (1886-1935) in an article entitled "Pseudo-Argyll Robertson Pupils with Absent Tendon Reflexes, a Benign Disorder Simulating Tabes Dorsalis," which appeared in the *British Medical Journal* (1:928-930, 1931). He writes:

I wish to draw attention to a benign symptomless disorder characterized by pupils which react on accommodation but not to light, and by absent tendon reflexes.

Five of the six cases I am about to describe came under my notice in the course of a few weeks; the condition therefore cannot be very rare. Though harmless in itself it merits recognition because it is often mistaken for a manifestation of syphilis of the nervous system, with unfortunate consequences for the patients and their families. . . .

. . . . The true Argyll Robertson pupil reacts promptly and fully, often excessively, on convergence, and dilates again as soon as the effort to converge the visual axes is relaxed. In these cases the pupils show the so-called myotonic reactions; they do not respond to light; they contract very slowly through a wide range during a sustained effort to converge; often remain small long after the effort ends, and, when they dilate again, do so slowly.

It seems to me more than probable that some . . . cases with non-luetic Argyll Robertson pupils but normal tendon reflexes are examples of a milder form of the same benign disorder that I have described here.

R. W. B.

OBITUARIES

CLARENCE JOHN BELL

1876-1943

He was the greatest Roman of them all.

It is difficult adequately to evaluate such a versatile personality as Dr. Bell. He typified the highest traditions of the country doctor. His casual mode of dress concealed an alert, well-disciplined mind and character. He had a direct incisive approach to everything he undertook. His medical skill and judgment was of such a character that he held a dominant position throughout his section of the Cape. Not only was he prominent professionally, but as a practical economist his opinion was widely sought. Dr. Bell was a director of the local bank, treasurer of the Methodist Church, a member for many years of the school board and an active supporter of "every good work."

Kindliness, tact and a love of his fellow man were conspicuous qualities that he possessed in full measure. The by-products of his practice, such as the payment of overdue mortgages without thought of personal recompense, and the successful solution of domestic difficulties among his patients, are legion. He possessed a delightful sense of humor, which colored all his dealings.

Wellfleet, to its everlasting credit, appreciating the man and his services, gave a public testimonial dinner in his honor two years ago. All who knew him genuinely mourn the passing of this noble soul.

Besides his wife, he leaves a daughter, Mrs. Stephen Daniel and a son, Richmond.

L. F. J.

MAURICE GERSTEIN

1870-1943

Maurice Gerstein, a practicing physician for forty five years, died suddenly on July 12, 1943, at Beth Israel Hospital, Boston. Born in Russia on March 1, 1870, he came to this country in 1888 and graduated from New York University Medical College in 1896.

He was a typical successful family doctor who gained the love and esteem of his patients. His records show that during his long practice he was the attending obstetrician in over five thousand deliveries. He was also successful as an organizer, having been a charter member and the first secretary of the medical staff of the former Mount Sinai Hospital, Boston, and a founder of the Greater Boston Bickur Cholim Hospital and the New Century Club. He was an ex president and supervising censor of the Norfolk District Medical Society and a member of the American Medical Association, the Greater Boston Medical Society and many charitable organizations.

During World War I, he volunteered in the Medical Service Corps, a local medical group, and was appointed chairman of the Soldier's Relief Commission in Ward 16.

Dr Gerstein was the author of several articles published in various medical journals. He was a founder of the former periodical *The Mount Sinai Monthly* and editor of *The Medical Directory of Greater Boston*, published in 1906.

His sudden death was a shock to his many associates, friends and relatives. He left a landmark in Boston medical and communal life, and died after a full, active and useful life.

S R K

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

CONNOR—THOMAS J. CONNOR, MD, of Arlington, died July 16. He was in his fifty-second year.

Dr Connor received his degree from the Boston University School of Medicine. He was a member of the Massachusetts Medical Society and the American Medical Association.

CURRAN—LOUIS F. CURRAN, MD, of Dorchester, died July 22. He was in his fifty-eighth year.

Dr Curran received his degree from Tufts College Medical School in 1917. At the time of his death, he was physician-in-chief of the medical department of the Carney Hospital and clinical professor of medicine at Tufts College Medical School. He was a member of the Massachusetts Medical Society, American Medical Association, American Gastroenterological Association, John Bottomley Medical Society, St. Luke's Medical Guild and the Louis Pasteur Medical Society.

He is survived by his widow, three sons and a sister.

JACKSON—ALTON A. JACKSON, MD, of Everett, died July 25. He was in his ninetyeth year.

Dr Jackson received his degree from Harvard Medical School in 1883. He was founder of the Whidden Memorial Hospital and the Everett Visiting Nurses Association. He was a member of the Massachusetts Medical Society and the American Medical Association.

Two sons and a daughter survive.

CORRESPONDENCE

RELOCATION OF PHYSICIANS

To the Editor: The following letter from a physician who has gone into a rural area that was lacking in medical services expresses so clearly and understandingly what has been and is being done throughout the country that I believe it deserves publication.

FRANK H. LAHEY, Chairman
Directing Board

Procurement and Assignment Service
War Manpower Commission
Washington, D C

• • •

Dear Dr. Lahey:

It has occurred to me that the following might interest you in connection with your procurement program.

I am sixty-seven years of age, and after specializing in urology for thirty years, came here in November at the request of the Board of Selectmen to take over the practice of the late Dr. Damon.

Wilbraham has a population of 3000 and covers 22 square miles. With the exception of a small Polish group, most of the people are middle-class Americans. The town has no hospital, no drugstore and no district nurse.

Because I was a member of the Massachusetts Medical Society and also came recommended by several well known medical men in Boston, I was accepted at once by the people, and in two weeks had all I could do.

There are several conclusions that I have arrived at in connection with a medical man past the Government age coming from the city into a country practice. First, it is not necessary or essential for him to make connections with a hospital in a nearby city. The people here wish to be sent to a specialist in Springfield in cases of serious illness, and the medical man has no time even to make a visit on his patient after turning him over to a Springfield consultant. Secondly, I believe that it is impracticable for an older medical man to assume the responsibility of practice in one of these towns unless he has kept up with modern medicine. It is amazing to learn the amount of knowledge the local people have of the newer drugs and newer methods of treatment. An important contributing factor to this is that the public schools have a number of medical examinations throughout the year at which the parents are present. And, finally, it is my opinion that the older medical man need not hesitate to practice in the country owing to fear of night work. The people are most considerate and believe that their doctor must be saved as much as possible from over work. Night calls, except in a rare emergency, can be handled over the telephone, and a call made the following morning. However he must be prepared to see a certain number of people in his office in the evening, since most

of the people are working during the day, and transportation presents difficulties.

The incoming doctor must make up his mind that at least 75 per cent of the work during the winter—November to April—consists of house calls. There are many reasons for this: severe illnesses, fear of contagious diseases on the part of patients, and the ever-increasing transportation problem. The doctor must take his time in his examinations, both in the home and in the office. The visit of the medical man is an event in many of their lives, and it must not be hurried. This is extremely important.

In conclusion, I believe that you, as head of the Procurement and Assignment Service, might help the overworked country medical man by publicizing the idea that the people should notify their medical man in the morning if they expect to see him the same day. I feel very strongly about this and hope that much publicity may be given to it. We country doctors work seven days a week; our meals are always interrupted, and we have little time with our families.

EDMUND L. SAUNDERS

Wilbraham, Massachusetts

NEW PREMARITAL BLOOD-TEST LAW

To the Editor: The following letter was recently forwarded to all physicians licensed to practice in Massachusetts.

VLADO A. GETTING
Commissioner of Public Health

State House
Boston

* * *

Dear Doctor:

A new premarital blood-test law has recently been passed and goes into effect immediately.

The new law (Section 28A of Chapter 207 of the General Laws) is essentially the same as the old, except for the following points, which we call to your attention:

(1) Under the new law the examination "shall be made only to ascertain the presence or absence of evidence of syphilis, and shall include a serological test for syphilis."

(2) The law now provides that the health certificate need not be presented until the time of issuance of the marriage license, and the examination and laboratory test must be made not more than thirty days before the date the *marriage license is issued*.

(3) The law now provides that the examination may also be made by "a physician registered or licensed to practice in any other state of the United States."

Until a new supply of forms is available, the old form will be accepted. We suggest that the section number in the next to the last line of the certificate be corrected to read "in accordance with section *twenty-eight A* of chapter two hundred and seven of the General Laws."

VLADO A. GETTING, M.D., Dr.P.H.
Commissioner of Public Health

BOOK REVIEWS

First Aid: Surgical and medical. By Warren H. Cole, M.D., and Charles B. Puestow, M.D., Ph.D. 8°, cloth, 351 pp., with 92 illustrations. New York: D. Appleton-Century Company, Incorporated, 1942. \$3.00.

This volume on surgical and medical first aid is one of the most complete that has ever been called to the reviewer's attention. The large number of contributing authors, each an expert in his subject, adds much to the value of the work. All the twenty-one chapters are worthy of most careful reading. Every conceivable question seems to be well covered, and the graphic illustrations are excellent. All the most important advances in the treatment of injuries, such as burns, with accompanying shock, and the correct methods for first aid in the treatment of fractures, are given most careful consideration, with helpful illustrations of transference of the injured with a minimum amount of disturbance and pain.

The first part of Chapter I, entitled "Precautions and Limitations in First-Aid Work," deserves particular attention. Here the question of errors in judgment is taken up. An instance of this is shown in the statement in which the authors truthfully say, "The indiscriminate use of the tourniquet of which first-aid workers are so frequently guilty is often an error in judgment." In the conclusion of this chapter the authors state: "We wish forcefully to remind the first-aid worker of the old proverb which warns us so truthfully that 'a little knowledge is a dangerous thing.' The first-aid worker must know his own limitations in knowledge and ability and abide by them."

This book well deserves a thorough and careful reading by all those who are interested in surgical and medical first aid.

Mental Health in College. By Clements C. Fry, M.D. With the collaboration of Edna G. Rostow. 8°, cloth, 365 pp. New York: The Commonwealth Fund, 1942. \$2.00.

The material covered in this book has been gathered in the last ten years by the Department of Psychiatry and Mental Hygiene at Yale University. A mental-hygiene service for students was first inaugurated in 1925 by Dr. Arthur Ruggles, but in the last ten years the work has been carried on by the author of this monograph. The book is a thorough study of mental disease as it appears in college students and is the best study of its type known to the reviewer.

The book is extremely well written, and the problems clearly set forth. There are illustrative case histories. The material was gathered not only from the undergraduate department but also from the postgraduate divisions of the university, where, incidentally, one is surprised to learn that there are so many mental maladjustments. The Commonwealth Fund has made this publication available at a reasonable price, and it is hoped that the book will be widely distributed. It can be recommended without reservation, and should be of use to all educators and to the medical profession in general.

(Notices on page viii)

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PROTHROMBIN DEFICIENCY IN BILIARY OBSTRUCTION AND DISEASES OF THE LIVER*

FREDA K. HERBERT, M.B., B.S.

NEWCASTLE-UPON-TYNE, ENGLAND

DURING the last seven years the explanation of the tendency to hemorrhage in diseases of the liver and biliary tract has been established, and satisfactory prophylactic measures are now available for patients with obstructive jaundice or biliary fistula. The maintenance of normal plasma prothrombin depends on an adequate supply and absorption of vitamin K. The actual relation between vitamin K and prothrombin formation is not clear, but it is known that prothrombin is formed in the liver, and that hypoprothrombinemia may result from lack of vitamin K, deficient absorption of the vitamin or gross damage to the liver parenchyma. In obstructive jaundice or biliary fistula the primary defect is in absorption, since vitamin K, like the fats and other fat-soluble substances, is not absorbed when bile salts are absent from the intestine. Therefore a large proportion of such cases show a low level of plasma prothrombin, and when this deficiency is serious there is a risk of hemorrhage following operation. The deficiency can be corrected by oral administration of bile salts, but this is a relatively slow process. The deficiency can be rapidly corrected by injection of vitamin K or its analogues, which are naphthoquinone derivatives. There are two naturally occurring vitamins. Vitamin K₁, derived from alfalfa, is 2-methyl-3-phytyl-1,4-naphthoquinone; vitamin K₂, derived from putrefied fish meal, is 2,3-difarnesyl-1,4-naphthoquinone. The phytyl and farnesyl side chains in these substances are not connected with their biologic activity, and several simpler naphthoquinones are as effective as the natural vitamins, or even more so. Apparently the most active analogue is 2-methyl-1,4-naphthoquinone, which is available for therapeutic use.

It has been established that estimations of plasma prothrombin often give warning of the risk of postoperative hemorrhage in cases in which there

is no spontaneous hemorrhage, and no abnormality in coagulation time or bleeding time. The estimation of prothrombin is therefore a useful clinical test, as showing when prophylactic treatment is necessary. However, there is usually a fall in plasma prothrombin following operations on the biliary tract, so that a normal value before operation does not necessarily exclude risk. Probably the main factor in this postoperative fall is manipulation of the liver (Lord¹ and Cullen, Ziffren, Gibson and Smith²).

In diseases of the liver associated with gross damage to the hepatic parenchyma, hypoprothrombinemia is of common occurrence, and is due not only to the defective absorption resulting from absence of bile from the intestine, but also to failure of the liver to manufacture prothrombin even when vitamin K is available. In such cases the plasma prothrombin does not rise in response to treatment with the vitamin. It is therefore necessary to bear in mind the possibility of associated liver disease in patients requiring operations on the biliary tract.

The evidence by which these facts were established has been reviewed by Brinkhous³ and by Butt and Snell.⁴ Recently numerous other authors have confirmed and extended observations on all the important points. Macfie, Bacharach and Chance⁵ reported the successful use of 2-methyl-1,4-naphthoquinone, given intramuscularly, in correcting hypoprothrombinemia in obstructive jaundice, and numerous authors⁶⁻¹⁸ have reported experience with this and with other naphthoquinone derivatives, which confirms the effectiveness of the treatment in obstructive jaundice and its failure in many cases of disease involving the hepatic parenchyma.

Methods for the estimation of plasma prothrombin fall into two categories—one-stage and two-stage technic. The one-stage type was introduced by Quick (Quick, Stanley-Brown and Bancroft¹⁹ and Quick²⁰) and has been popular on account of

*From the Department of Pathology, the Medical School, King's College, and the Royal Victoria Infirmary Newcastle upon Tyne, England.

its simplicity. It depends on the time taken to form a clot when suitable amounts of calcium and thromboplastin are added to plasma. During the short time required for coagulation, only a very small proportion of the plasma prothrombin is converted into thrombin; the clotting time depends on the rate of thrombin formation. The rate of formation of thrombin depends on the prothrombin titer, and the clotting times obtained with any given plasma can be expressed in terms of prothrombin titers by comparison with a calibration curve based on serial dilutions of normal plasma. There have been many modifications of the one-stage procedure, some designed to give a rapid and simple means of detecting serious prothrombin deficiency, and others aiming at greater accuracy. For the maximum accuracy it is essential to use serial dilutions not only of the normal standard plasma but also of the plasma to be tested. Careful standardization of thromboplastin is also necessary. All methods of the one-stage type are, however, open to the objection that they are based on the rate of formation of thrombin from prothrombin, and that this may be affected by other factors besides the prothrombin titer. These other factors are especially important when comparisons are made between different species, or between infants and adults.

This difficulty is avoided in the two-stage method introduced by Warner and his associates (Warner, Brinkhous and Smith²¹ and Smith, Warner and Brinkhous²²). In this method the plasma, in high dilution, is treated with calcium and thromboplastin and incubated until thrombin activity is maximal. The thrombin formed is then estimated from the time taken for formation of a clot with added fibrinogen. This is much more satisfactory in principle than the one-stage method. The factors involved in it have been studied by me^{23, 24} and a modification described.

The present paper describes experience with the two-stage method of estimating plasma prothrombin in obstructive jaundice and diseases of the liver. Its main contribution to the subject is additional evidence concerning the incidence of hypoprothrombinemia in these conditions, based on an accurate technic. There are also examples of the correction of the prothrombin deficiency by treatment in cases of obstructive jaundice, and the lack of response in liver diseases. Plasma phosphatase has been estimated in a large proportion of the cases by the method of Jenner and Kay,²⁵ and in some cases the diagnosis was assisted by the use of the levulose tolerance test, with analyses of blood levulose (Herbert²⁶).

RESULTS

Biliary Obstruction

In all, 79 cases of obstructive jaundice have been examined. In 18 of these the jaundice was only slight, with the serum bilirubin not more than 2.4 mg. per 100 cc., and among these there were only 3 cases of prothrombin deficiency. These showed prothrombin titers of 68, 73 and 74 per cent of the normal average (normal range, 80 to 120 per cent of normal average). There were also 10 cases that were first examined after treatment had begun. Although some of these will be referred to later, they are excluded from the main table.

The remaining 51 cases, with moderate or intense jaundice, are described in Table 1. The prothrombin titers are those found before treatment was given. They were normal in only 16 cases, the remainder being between 50 and 80 per cent of normal in 19 cases, and less than 50 per cent of normal in 16 cases.

There is no regular correlation in this group between serum bilirubin and prothrombin, or between phosphatase and prothrombin. Although, in general, severe and long-standing biliary obstruction tends to yield the highest phosphatase and lowest prothrombin titers, there is no constant association between high phosphatase and low prothrombin in single cases. Close correlation could hardly be expected, because even if the severity and duration of obstruction were the only factors affecting the rise in phosphatase (which is uncertain), the prothrombin would be affected also by other factors. There may have been coincidental liver damage in some cases, and variations in the vitamin K intake may have had some effect where obstruction was partial or intermittent and absorption not entirely suppressed.

There is a definite relation between the prothrombin titer and the duration of obstruction. This point is best shown by considering obstruction due to malignant disease, since in these cases it was persistent. Malignant disease was the cause of obstruction in Cases 9 to 41, inclusive, which are listed in Table 1 in order of the duration of jaundice. They may be conveniently considered in two groups—one of 19 cases in which jaundice had been present for not more than four weeks, and one of 14 cases with longer duration of jaundice. The range of prothrombin titers in the first group is 31 to 119 per cent of normal, with an average of 76 per cent. That in the second group is 14 to 76 per cent of normal, with an average of 45 per cent. In the first group, 8 of the 19 cases showed normal values, and only 4 had values below 50 per cent of normal, whereas in the second group none were normal and 10 of the

14 cases showed titers below 50 per cent. Thus, *Treatment.* At the beginning of the present study a few patients were treated by the oral ad-

TABLE 1. Summary of Data in Cases with Biliary Obstruction.

CASE NO.	AGE	DIAGNOSIS	PLASMA BILI RUBIN* mg/100 cc	PLASMA PROTHROMBIN % normal	PLASMA PHOSPHATASE units	DURATION OF JAUNDICE	CONFIRMATION OF DIAGNOSIS
	yr.						
1	49	Gallstones	4.8	80	3.1	1 day	Operation
2	57	Gallstones	3.2	66	8.4	?	Operation
3	47	Gallstones	3.2	119	16.2	5 days	Operation
4	55	Gallstones	6.4	80	—	10 days	Operation
5	63	Stone in common duct	8.4	68	—	14 days	Operation
6	49	Gallstones, fistula between gall bladder and colon	3.2	62	37.0	14 days	Operation
7	63	Stone in common duct	8.0	70	48.2	13 wk (intermittent)	Operation
8	68	Gallstones and early carcinoma of gall bladder	14.4	24	50.4	10 wk	Operation
9	67	Carcinoma	4.8	108	13.8	3 days	Clinical data
			6.4	97	13.8	13 days	
10	53	Carcinoma of gall bladder	8.6	110	9.5	4 days	Operation
				62†			
11	47	Carcinoma of stomach	4.8	31	83.0	7 days	Postmortem
12	61	Carcinoma of pancreas	14.0	87	32.7	10 days	Operation
13	65	Carcinoma of pancreas	16.0	112	22.0	2 wk	Operation
				38†			
14	62	Secondary carcinoma of liver	4.8	59	18.0	2 wk	Clinical data
15	?	Carcinoma of gall bladder	7.2	59	29.4	2 wk	Operation
16	42	Carcinoma of pancreas	2.4	31	41.4	2 wk	Operation
17	46	Carcinoma of stomach and liver	9.6	72	45.6	2 wk	Postmortem
18	64	Carcinoma of pancreas	16.8	91	28.2	16 days	Operation
19	60	Carcinoma of gall bladder and liver	8.0	47	—	3 wk	Operation
20	74	Carcinoma of pancreas	6.4	57	7.8	3 wk	Clinical data
			8.0	57	18.0	8 wk	
21	54	Carcinoma of ampulla of Vater	12.8	63	10.2	4 wk	Operation
22	51	Carcinoma of pancreas	8.0	35	24.0	4 wk	Operation
23	82	Carcinoma of ampulla of Vater	11.2	76	26.4	4 wk	Operation
24	65	Carcinoma of pancreas	14.4	113	39.2	4 wk	Clinical data
25	68	Carcinoma of ampulla of Vater	4.8	107	40.0	4 wk	Operation
26	68	Carcinoma of pancreas	8.0	76	42.2	4 wk	Operation
27	54	Carcinoma	8.0	119	45.6	4 wk	Clinical data
28	59	Carcinoma of bile ducts	9.6	49	59.4	5 wk	Postmortem
29	53	Carcinoma of pancreas	11.2	67	72.0	5 wk	Operation
30	62	Carcinoma	15.2	53	—	6 wk	Clinical data
31	58	Carcinoma of pancreas	8.0	42	—	6 wk	Clinical data
32	44	Secondary carcinoma of liver	High	43	—	7 wk	Clinical data
33	40	Carcinoma of pancreas	4.8	76	29.4	8 wk (intermittent)	Operation
34	69	Carcinoma	9.6	47	33.0	8 wk	Clinical data
35	66	Carcinoma of pancreas	5.6	20	49.5	8 wk	Operation
36	61	Carcinoma of gall bladder and liver	11.2	53	24.6	4 mo	Operation
37	54	Carcinoma of ampulla of Vater, gallstones and biliary cirrhosis	12.8	14	81.0	4 mo	Postmortem
38	?	Carcinoma of pancreas	7.2	21	34.8	5 mo	Clinical data
39	61	Carcinoma of pancreas	9.6	62	49.0	6 mo	Operation
40	69	Carcinoma of ampulla of Vater	18.4	42	75.0	6 mo	Operation
41	72	Carcinoma of pancreas	8.0	45	110.0	8 mo	Operation
42	58	Carcinoma of gall bladder		27†	—		Operation
43	64	Obstructive jaundice	32.0	112	—	8 days	Clinical data
44	61	Obstructive jaundice	12.8	62	—	2 wk	Clinical data
45	63	Obstructive jaundice	12.8	59	32.4	2 wk	Clinical data
46	50	Lymphadenoma	11.2	31	63.6	2 wk	Postmortem
47	64	Chronic pancreatitis	8.0	119	17.4	18 days	Operation
48	45	Obstruction by glands	4.8	91	14.4	3 wk	Operation
49	59	Chronic pancreatitis	14.0	91	55.8	3 wk	Operation
50	70	Obstructive jaundice	4.4	88	54.6	7 wk	Clinical data
51	64	Obstructive jaundice	16.0	58	22.2	6 wk	Clinical data

*Plasma bilirubin in all cases gave the direct van den Bergh reaction.

†Bleeding after operation.

at an early stage, it is usual during the first four weeks to find normal or moderately low values, whereas after four weeks the titers are all low and the grosser deficiencies much more frequent.

ministration of bile only. This corrected the prothrombin deficiency, but the return to normal was slow. In Case 40, the prothrombin titer before treatment was 42 per cent of normal. After

days' treatment with bile salts it was 34 per cent, and later it gradually rose, reaching 75 per cent on the eleventh day of treatment and 116 per cent on the fifteenth day. In Case 5, the level of prothrombin before treatment was 68 per cent. After nine days' treatment with bile salts it had reached 105 per cent. In Case 8, the initial level was 24 per cent of normal. After five days of bile treatment it was 17 per cent; it then gradually rose, reaching 45 per cent on the twelfth day. On the evening of the twelfth day the patient had an injection of 2-methyl-1,4-naphthoquinone (Kapilon) and the next morning the prothrombin level was 64 per cent. After this, one more injection of the naphthoquinone was given; the prothrombin was not estimated again, but operation was performed without any hemorrhagic complication.

Early in the course of this study, treatment by intramuscular injections of 2-methyl-1,4-naphthoquinone was adopted throughout the hospital before operation and in the postoperative period, as well as for some patients who were not operated on. In obstructive jaundice the treatment regularly caused a rise in plasma prothrombin. In Case 29, the prothrombin level rose from 67 to 99 per cent; in Case 22, from 35 to 118 per cent; in Case 19, from 47 to 100 per cent; in Case 35, from 20 to 77 per cent; in Case 37, from 15 to 64 per cent; in Case 15, from 59 to 100 per cent; and in Case 42, from 27 to 76 per cent. The time required for full restoration varied, and in some cases estimations were not made frequently enough to show the rate of response. Where estimations were made at short intervals, they showed that some response was obtained very early. In Case 35, the plasma prothrombin level before treatment ranged from 19 to 21 per cent; four hours after the first dose of 1 cc. of Kapilon* it had risen to 34 per cent; the patient then received 2 cc. daily (except for an omission on the fourth day) and the level rose gradually to 77 per cent by the tenth day. In Case 37, the level before treatment was 15 per cent and seven hours after the first dose of Kapilon it had risen to 49 per cent. Case 42 showed a rapid response. The first observation was made when the patient was suffering from postoperative hemorrhage and the plasma prothrombin was 27 per cent of normal. At 11 a.m. on the following day she was given 1 cc. of Kapilon. At 4 p.m. there was still some oozing from the wound and the plasma prothrombin was 64 per cent. There was less oozing during the following night; the next morning the prothrombin level was 76 per cent and the hemorrhage was controlled.

*One cubic centimeter contains 5 mg. of 2-methyl-1,4-naphthoquinone.

In only 1 case of obstructive jaundice (Case 31) was the response unsatisfactory. Before treatment, the prothrombin titer was 42 per cent of normal. The patient was given 1 cc. of Kapilon daily; on the second day of treatment the prothrombin was 55 per cent of normal, and on the fourth day, 51 per cent. The diagnosis was carcinoma of the pancreas, and since there was enlargement of the liver and ascites, it seems probable that the lack of response to treatment was due to invasion of the liver by secondary growth.

Hemorrhage. None of the patients with obstructive jaundice showed spontaneous hemorrhage on clinical observation. There were 2 fatal cases, not suitable for operation, in which some hemorrhage without anatomic cause was found at autopsy. One of these patients (Case 46) had lymphadenoma, with obstruction to the pancreatic duct by lymph nodes, together with cholecystitis, gallstones and terminal acute pancreatitis. The plasma prothrombin level was 31 per cent of normal and there was hemorrhage from the gastrointestinal tract. The other patient (Case 11) had a carcinoma of the pyloric end of the stomach, with obstruction to the common bile duct and secondary carcinoma of the liver and lungs. The plasma prothrombin was 31 per cent of normal, and there was a hemorrhage into the pelvis of one kidney.

It is generally agreed that spontaneous hemorrhage occurs only with gross deficiencies in prothrombin, and that the main danger is postoperative hemorrhage. This was rarely seen in the present study because, with one exception, all patients showing low prothrombin levels, and several who had normal levels were given prophylactic and often postoperative treatment. In all, 53 cases of obstructive jaundice came to operation; only 7 had abnormal postoperative bleeding, and in 3 of these it was slight.

In Case 42, already mentioned, the prothrombin had not been estimated before operation and no treatment had been given. There was bleeding from the wound after operation, with the plasma prothrombin 27 per cent of normal. Treatment with naphthoquinone quickly restored the prothrombin level and controlled the bleeding.

In Case 16, the original level of prothrombin was 31 per cent of normal. The patient had a week's course of naphthoquinone injections before operation (cholecystgastrostomy), but no further prothrombin estimations were made before the operation. On the third day after operation there was slight oozing from the wound. The next day the plasma prothrombin was 65 per cent of normal; the oozing had then ceased.

In the other 5 cases with postoperative bleeding, the prothrombin had been found normal before operation, either without treatment or after treatment. In Case 10, the preoperative prothrombin level was 110 per cent of normal, and at the time of postoperative bleeding 62 per cent. Naphthoquinone was given at this stage and the bleeding controlled. In Case 13, the preoperative prothrombin level was 112 per cent of normal. No preoperative treatment was given, and bleeding occurred four days after the operation, with the plasma prothrombin 38 per cent of normal. The patient died. These cases confirm the observations of other workers that the prothrombin level may fall after operation and that a normal preoperative level does not exclude risk. The 3 other patients were known to have normal prothrombin titers before operation, but the estimation was not made at the time of bleeding. In 2 of them the oozing was only slight, and since both had chronic cholecystitis with adhesions, the cause may have been anatomic.

So far as can be judged from these few cases, it appears that postoperative hemorrhage is likely to occur when the plasma prothrombin is 60 per cent or lower.

Diseases of Liver

The results in 40 cases of liver disease are shown in Table 2. Of these, 27 showed deficiency in plasma prothrombin.

In acute or subacute hepatitis of various types (Cases 52 to 69, inclusive), the titers ranged from 17 to 106 per cent of normal. Seven out of the 18 cases showed normal results, and most of the remainder showed moderate deficiencies, only 3 having titers below 56 per cent of the normal average. None of the 3 cases of Weil's disease showed any gross hemorrhagic tendency; there were no hemorrhages in Case 69, only slight hemorrhages in the gums in Case 67, and slight purpura in Case 68. There was 1 case in this group with gross hemorrhage, namely Case 66. This patient had several courses of antisyphilitic treatment (arsenicals and bismuth) between December, 1940, and July, 1941. In October, 1941, he was admitted to the hospital severely ill and jaundiced and died on the day of admission from *Clostridium welchii* septicemia and peritonitis. There were extensive hemorrhages in the serous cavities, endocardium and intestines, and histologically the liver showed evidence of successive phases of toxic damage, attributable to the arsenical treatment. The plasma prothrombin level a few hours before death was 19 per cent of normal.

In 2 cases of liver atrophy (Cases 73 and 74), there was severe prothrombin deficiency, and in

2 cases of post atrophic fibrosis (Cases 78 and 79), there was considerable deficiency.

There were 12 cases of cirrhosis of the liver (Cases 80 to 91, inclusive). Only 3 of these showed normal prothrombin levels, but the deficiencies in the remainder were usually slight, the titer falling below 50 per cent of normal in only 2 cases.

In 15 of the 40 cases of liver disease, a levulose tolerance test was performed. When this test is based on analyses of blood levulose, the maximum normal rise is 15 mg per 100 cc and most normal subjects show rises of no more than 10 mg per 100 cc. Results in the range of 10 to 15 mg per 100 cc. may be regarded as borderline. In 3 cases (Cases 55, 58 and 86), the rise in blood levulose was less than 10 mg per 100 cc. The prothrombin titers were 80, 106 and 92 per cent of normal, respectively. Four cases (Cases 61, 65, 82 and 91) showed borderline results. The prothrombin titers were 86, 88, 70 and 73 per cent of normal, respectively. Of the cases with deficient levulose tolerance, 3 (Cases 62, 81 and 89) had moderately reduced tolerance, with rises of blood levulose of 15 to 25 mg per 100 cc. The prothrombin titers were 75, 72 and 113 per cent of normal, respectively. There were 5 cases (Cases 63, 64, 74, 84 and 87) showing gross deficiency in levulose tolerance, with rises of greater than 25 mg per 100 cc. The prothrombin titers were 53, 57, 36, 70 and 33 per cent of normal, respectively.

In this small series, therefore, the prothrombin fell below 70 per cent of normal only when the levulose test showed gross deficiency.

Effects of Treatment

Several authors have pointed out that hypoprothrombinemia associated with damage to the hepatic parenchyma does not respond to treatment with vitamin K or its analogues. The present study affords examples of this lack of response. One case (Case 31) has already been mentioned in which a poor response was attributed to secondary carcinoma of the liver.

In 5 of the cases listed in Table 2 the effect of injections of naphthoquinone was tried. In Cases 60 and 64 there was some rise in plasma prothrombin, but the patient was improving at the time and the rise in prothrombin may have been due as much to natural recovery as to treatment. In the other 3 cases (Cases 74, 85 and 87) there was no response. The first (Case 74) was a case of subacute liver atrophy with grossly deficient levulose tolerance. The initial level of plasma prothrombin was 36 per cent of normal, and after daily injections of naphthoquinone for twelve days it was 38 per cent. The other 2 (Cases 85 and 87) were cases of cirrhosis. The

levulose tolerance was not estimated in Case 85; it was grossly deficient in Case 87. In Case 85, 1 cc. of Kapilon was given daily for six days, and the prothrombin titers before and after treatment were 54 and 52 per cent, respectively. In Case 87,

similar to those obtained by Brinkhous, Smith and Warner²⁷ and by Stewart and Rourke²⁸ with the two-stage method, although there is a slightly higher proportion of normal results in the present series. The three series of results are not quite

TABLE 2. Summary of Data in Cases with Liver Disease.

CASE No.	AGE	DIAGNOSIS	PLASMA BILI- RUBIN*	PLASMA PRO- THROMBIN	PLASMA PHOSPHATASE	DURATION OF JAUNDICE	CONFIRMATION OF DIAGNOSIS
	yr.		mg./100 cc.	% normal	units		
52	40	Acute hepatitis	8.0	43	15.0	5 days	Clinical data
53	40	Acute hepatitis	6.4	81	6.0	5 days	Clinical data
54	22	Acute hepatitis	8.0	56	9.0	9 days	Clinical data
55	11	Acute hepatitis (epidemic)	3.6	80	—	9 days	Clinical data
56	39	Acute hepatitis	8.0	59	18.6	11 days	Clinical data
57	26	Acute hepatitis	2.0	82	—	14 days	Clinical data
58	22	Acute hepatitis	4.0	106	9.0	14 days	Clinical data
59	55	Acute hepatitis (epidemic)	8.0	69	16.8	4 wk.	Clinical data
60	31	Acute hepatitis	9.6	17	12.8	5 wk.	Clinical data
61	81	Acute hepatitis	1.2	86	7.2	6 wk.	Clinical data
62	10	Subacute hepatitis	4.8	75	—	3 mo.	Clinical data
63	22	Subacute hepatic necrosis	1.2	53	—	3 mo.	Clinical data
64	55	Subacute hepatitis	8.0	57	18.0	4 mo. (intermittent)	Clinical data
65	14½	Subacute hepatitis	8.4	88	11.4	6 mo.	Clinical data
66	42	Toxic hepatitis (arsenical) and terminal <i>Cl. welchii</i> infection	6.0	19	—	—	Postmortem
67	46	Weil's disease	11.0	86	—	10 days	Agglutination test
68	39	Weil's disease	12.8	69	—	11 days	Agglutination test
69	52	Weil's disease	7.2	64	—	16 days	Agglutination test
70		Septic hepatitis	16.8	104	—	—	Postmortem
71	13	Pyemic abscesses in liver	9.6	42	—	2 wk.	Postmortem
72	78	Infective cholangitis	10.4	70	6.0	9 days	Operation
73	26	Acute yellow atrophy (arsenical)	9.6	20	—	1 wk.	Postmortem
74	40	Subacute atrophy of liver	2.0	36	11.4	3 wk.	Clinical data
75	40	Myocarditis, congestion and necrosis of liver	9.6	97	—	?	Postmortem
76	42	Cardiac failure and congestion of liver	5.6	69	—	?	Clinical data
77	34	Infective endocarditis and jaundice	6.0	85	—	3 days	Postmortem
78	55	Post-atrophic fibrosis of liver	6.4	55	16.2	—	Postmortem
79	61	Post-atrophic fibrosis of liver	3.2	47	—	3 days	Postmortem
80	62	Cirrhosis of liver	Normal	75	7.2	5 wk.	Operation
81	64	Cirrhosis of liver	—	72	—	?	Clinical data
82	57	Cirrhosis of liver	Normal	70	—	?	Clinical data
83	44	Cirrhosis of liver	4.0	46	30.6	?	Clinical data
84	37	Cirrhosis of liver	Normal	70	—	?	Clinical data
85	47	Cirrhosis of liver	1.2	54	—	?	Clinical data
86	30	Cirrhosis of liver ³	0.2	92	—	?	Clinical data
87	39	Cirrhosis of liver	11.2	33	12.0	?	Clinical data
88	60	Gallstones and biliary cirrhosis	2.4	134	52.8	2 wk.	Operation
89	44	Biliary cirrhosis	2.0	113	59.4	10 mo.	Clinical data
90	55	Biliary cirrhosis	8.0	71	16.2	3 yr.	Operation
91	52	Biliary cirrhosis (gallstones)	9.6	73	10.8	6 wk.	Operation

*Plasma bilirubin gave the direct van den Bergh reaction in all cases except those described as normal.

2 cc. of Kapilon was given daily for seven days, and the prothrombin titer, 33 per cent of normal, was exactly the same before and after treatment.

SUMMARY AND CONCLUSIONS

The incidence of prothrombin deficiency in obstructive jaundice has been estimated by the two-stage technic in a series of 51 cases with serum-bilirubin levels over 2.4 mg. per 100 cc. Of these, 68 per cent showed hypoprothrombinemia, and in 30 per cent the titers fell below 50 per cent of the normal average. These results are closely

comparable, owing to differences in technic and in clinical material, but they do not differ greatly.

In 40 cases of liver disease studied in the present series, 68 per cent showed hypoprothrombinemia, and in 25 per cent the titers fell below 50 per cent. In some cases hypoprothrombinemia was found when the jaundice was extremely slight.

Cases are given of the restoration of the plasma prothrombin level to normal by treatment with 2-methyl-1,4-naphthoquinone in patients with biliary obstruction, and of the failure of this treat-

ment when there was damage to the hepatic parenchyma

In common with other authors, it was found that patients with a normal plasma prothrombin before operation may develop hypoprothrombinemia and hemorrhage a few days after operation

I am indebted to the honorary medical and surgical staff of the Royal Victoria Infirmary for the opportunity to investigate patients under their care and for the use of their clinical notes, and to my colleagues on the pathological staff for the use of their post mortem records

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VENOUS PRESSURE IN THE LOWER EXTREMITIES DURING ABDOMINAL OPERATIONS*

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BOSTON

THE frequent occurrence of postoperative thrombophlebitis of the femoral and leg veins makes it important to obtain data bearing on the state of the venous circulation in the legs during operation. Since such data are scanty it was decided to study the venous pressure in the leg veins during abdominal operations. Certain studies de-

minute intervals during abdominal operations. Following general or spinal anesthesia, these veins are usually prominent and admit an 18-gauge needle. A citrated 0.2 to 0.8 per cent solution of sodium chloride was used. Routine operative procedures were in no way altered during these observations. With each change in position, the

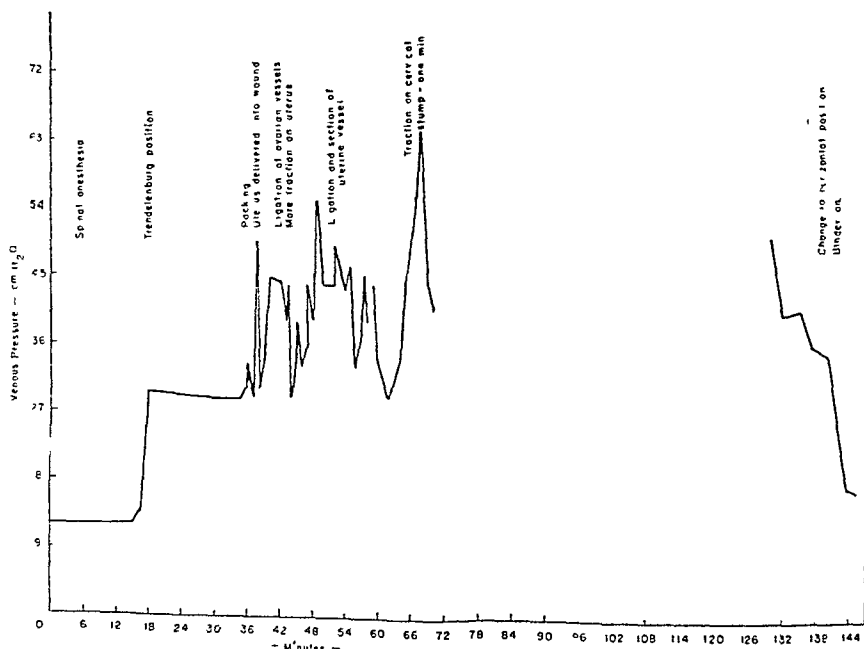


FIGURE 1. *Hysterectomy (spinal anesthesia).*

signed to elucidate the origin of the changes observed were also made.

MATERIAL AND METHODS

Studies were made in 18 cases. Ten patients had operations on the uterus, the procedures consisting of subtotal hysterectomy in 8 cases, pan-hysterectomy in 1 and presacral neurectomy with uterine suspension in 1; 4 patients underwent cholecystectomy, and 4 unilateral herniorrhaphy.

The venous pressure was measured by the method of Moritz and von Tabora¹ in one of the superficial veins of the foot at approximately one-

distance from the surface of the operating table at the heart level to the floor was measured and the angle of the table recorded. In the horizontal position, the point of reference was taken as 10 cm. above the surface of the table,² while in the Trendelenburg position the location of the left auricle was estimated. Using this estimated position as a point of reference, it was found that the manometer reading increased proportionally as the degree of the Trendelenburg position increased. According to Clark, Hooker and Weed,³ this increase is a hydrostatic effect due to the changing position of the true point of reference, which is no longer the auricle. The same change can be obtained in dead animals. In the present studies, therefore, only increases for a given position were considered significant. The position of the legs, whether extended or flexed at the knees, did not appreciably

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alter the manometer reading for any given position of the table

OBSERVATIONS

Operations on the Uterus

Appreciable increases in venous pressure in the leg occurred during some stage of the ten opera-

tures at this period of the operation were generally close to the preoperative values, they were often slightly higher and at times, as noted above, considerably above the preoperative levels

In 8 of the 10 cases, the increases were of the same general magnitude, that is, 15 to 30 cm (Figs 1, 2, 5, 6 and 7) In 2 others (Figs 3 and

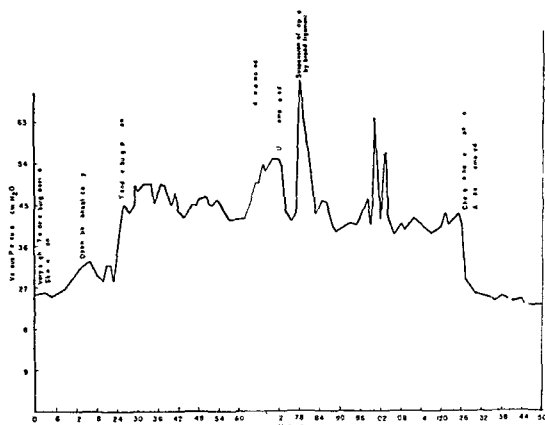


FIGURE 2 *Hysterectomy (nitrous oxide oxygen and ether anesthesia)*

tions on the uterus. In certain cases they were marked and prolonged (Figs 1-7). The first sharp change in the curve in 3 cases (Figs 1, 2 and 3) was due to a change in the base line following a shift from the horizontal to the Trendelenburg position. Rises above this level, however, represent true increases in venous pressure. Such increases sometimes followed the introduction of packs and exploration of the abdominal cavity, but this did not occur regularly. Marked rises in venous pressure, however, occurred in almost all cases when traction was placed on the uterus or its adnexa during isolation and ligation of the uterine and ovarian vessels. The rises generally persisted as long as the uterus was held ante flexed or under traction. The degree of tension that the surgeon was applying at a given moment could not, however, be estimated with accuracy.

The venous pressure generally fell sharply when traction on the uterus was released, although it did not always immediately return to previous levels. In 2 cases (Figs 4 and 5), the return to lower levels was gradual following amputation of the uterus. A similar elevation in venous pressure at the close of the operation is noted in another case (Fig 6). Although the venous pres-

sure at this period of the operation were generally close to the preoperative values, they were often slightly higher and at times, as noted above, considerably above the preoperative levels.

Cholecystectomy

In 2 of the 4 cases of cholecystectomy the venous pressure showed little change during operation. Appreciable increases occurred, however, in the course of the other 2 during exploration of the common duct, packing and various preparations for roentgenography (Figs 8 and 9). The application of the abdominal binder did not cause an increase in venous pressure.

Herniorrhaphy

In the 4 operations for herniorrhaphy, the venous pressure was measured in the veins of the foot on the side of operation. Few changes were noted. In one case, however, there was a marked increase at the time the conjoint tendon was sutured to Poupart's ligament. In another there were intermittent rises of 5 to 10 cm above the initial pressure.

The application of the adhesive dressing and abdominal binder at the end of operation was, however, accompanied in 3 cases by a persistent

increase in venous pressure of 3, 9 and 14 cm., respectively (Fig. 10). In the last case a rise of 5 cm. was noted when the dressing was applied, and with the application of the binder there was a further rise of 9 cm. This total increase of 14 cm. persisted for the thirty minutes that observations were permitted. Three hours later the venous pressure had returned to normal.

DISCUSSION

Veal and Hussey,⁴ in the course of ten abdominal operations performed for a variety of condi-

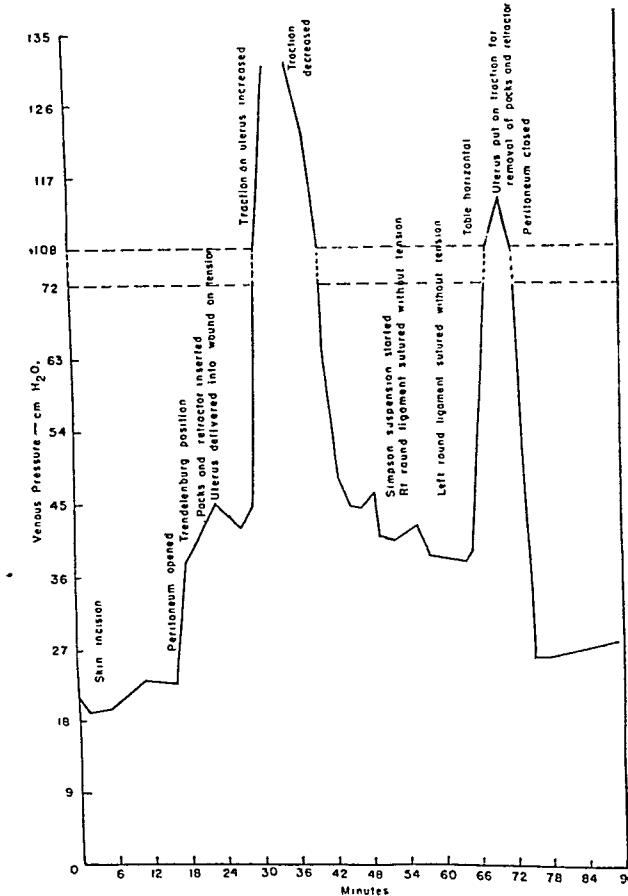


FIGURE 3. Presacral Neurectomy and Simpson Suspension (nitrous oxide, oxygen and ether anesthesia).

tions, measured venous pressure simultaneously in the antecubital vein of the arm and in the great saphenous vein close to its opening into the femoral vein. They were not impressed with the magnitude of the changes noted, although in 2 cases of hysterectomy there were maximum increases in the saphenous vein of 14 and 18 cm., respectively, above the preoperative level.

The data presented here, however, show far greater increases, particularly in the course of certain operations. The three types of operation selected for this study were chosen because the incidence of postoperative thrombophlebitis is different in each. In a recent study, for example, Barker,

Nygaard, Walters and Priestley⁵ found the incidence of postoperative thrombosis and embolism

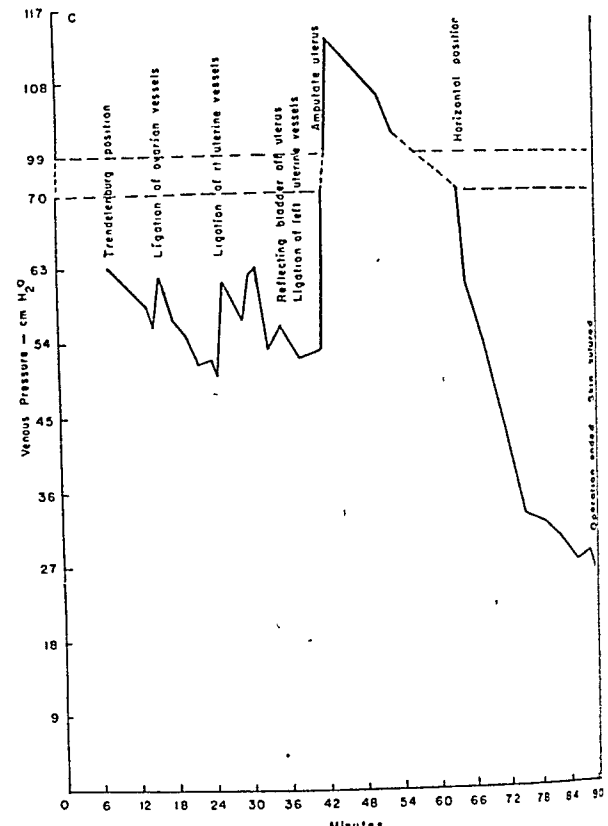


FIGURE 4. Hysterectomy (ether anesthesia).

to be 4.1 per cent for abdominal hysterectomy, 2.1 per cent for cholecystectomy and 1.3 per cent for

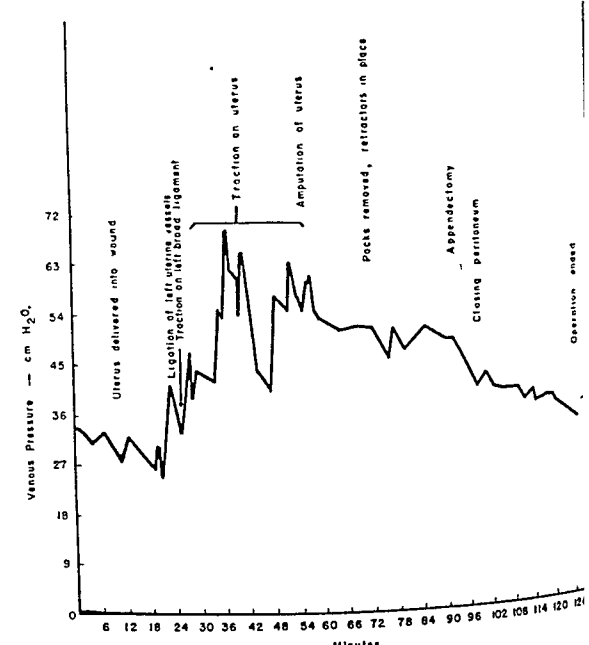


FIGURE 5. Hysterectomy (spinal anesthesia).

unilateral inguinal or femoral herniorrhaphy. The severity and frequency of the changes in veno

pressure noted in our study corresponded roughly with this relative incidence

In Veal and Hussey's study, the pressure in the antecubital vein was generally unaffected by manipulations that produced an immediate elevation

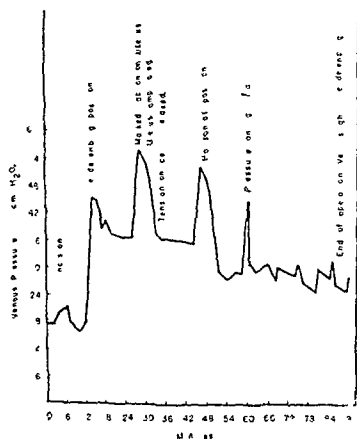


FIGURE 6 Hysterectomy (spinal anesthesia)

in pressure in the sphenous vein. It appears, therefore, that the changes that we obtained in the leg vein were not related to any general increase in venous pressure and that locally acting phenomena must be considered. The increases in venous pressure following the insertion of packs or traction on a viscus might have resulted from mechanical obstruction of the vena cava or the great veins of the pelvis. Since marked rises occurred during operations on the uterus, it was considered that the iliac veins might become kinked as a result of tension on the broad ligament. Anatomically there is a close relation between the lateral ends of the broad ligament and the iliac vessels. Traction on the lateral attachments of the broad ligament during three operations while the uterus and adnexa were still in their normal positions did not appreciably affect the venous pressure in the corresponding extremity, all these patients showed the usual increases later in the course of hysterectomy. Accordingly, kinking of the iliac vein does not appear to be a likely explanation for the rise in venous pressure during hysterectomy. Direct pressure on the vein, however, may still be a factor.

Many of our patients received Neo Synephrine during the operation. At times, its administration was followed by rises in venous pressure of 1 to 3 cm. On other occasions, however, there was

little or no rise. The major changes in venous pressure recorded in these studies were not related in time to the use of this drug.

A possible explanation for the rise in venous pressure is suggested by previous studies on the response of the veins to stimulation. It has been known for a long time that veins respond by contraction or dilatation to various stimuli or the action of drugs. In 1893, Thompson⁶ observed spindle-like constrictions of the external sphenous vein in rabbits and dogs following stimulation of the sciatic nerve. The constriction did not extend throughout the exposed vein, but was limited to certain segments between which the caliber remained unchanged. A few years later Bancroft⁷ observed the same phenomenon in cats and rabbits and traced the origin of the venomotor nerves to the spinal cord. He ruled out the possibility that

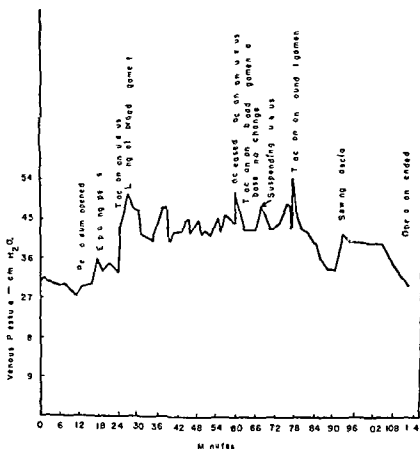


FIGURE 7 Bilateral Uteral Resection of Ovaries and Suspension of Uterus (spinal anesthesia)

this constriction was due to the contraction of skeletal muscles by the use of curare. Stimulation of the peripheral end of the severed nerve with a weak interrupted induction current produced marked, irregularly localized constrictions. In the rabbit, segments as long as 30 to 40 mm. and in the cat even longer lengths were observed to contract uniformly. That these venous responses were not secondary to changes on the arterial side of the circulation was proved by Ducessin⁸ who, after clamping the femoral artery and connecting the central end of the internal sphenous vein with a manometer, stimulated the anterior crural nerve and observed a rise in venous pressure. Hooker⁹

stimulated the nerve accompanying the inferior mesenteric artery and obtained manometric evidence of constriction of the mesenteric vein. The vena cava between entries of the iliac and renal veins. Recently Davis and Freedberg¹² have made venographic studies by means of Diodrast before

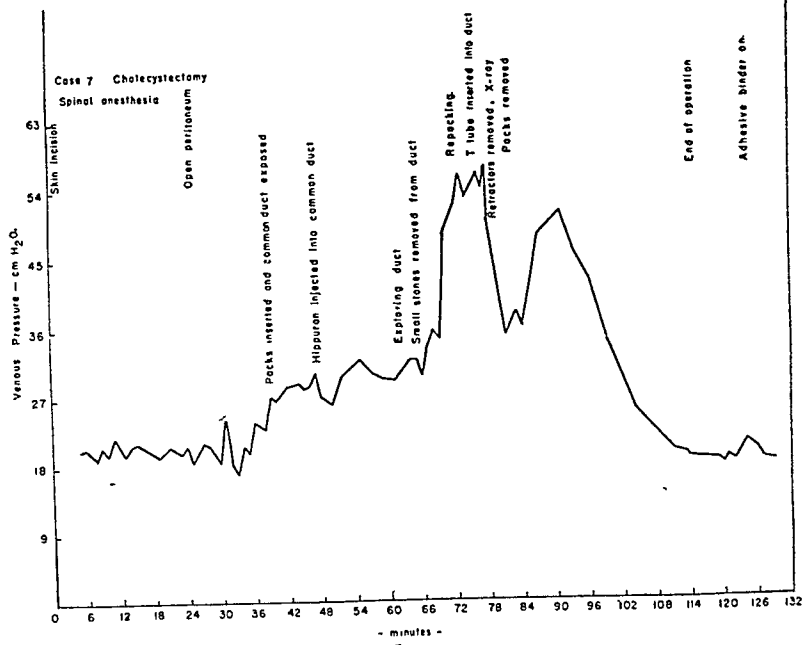


FIGURE 8. Cholecystectomy (spinal anesthesia).

same result was obtained by stimulating the vasomotor center directly by asphyxia and reflexly by stimulation of the central end of a sensory nerve. Donegan¹⁰ reinvestigated the question in the cat and obtained additional data confirming and extending the results of Franklin and Donegan⁹ and after stimulation of the sciatic nerve. Figure 11 shows marked narrowing of the saphenous vein following stimulation of the peripheral cut end of the sciatic nerve. Although definite conclusions cannot be drawn

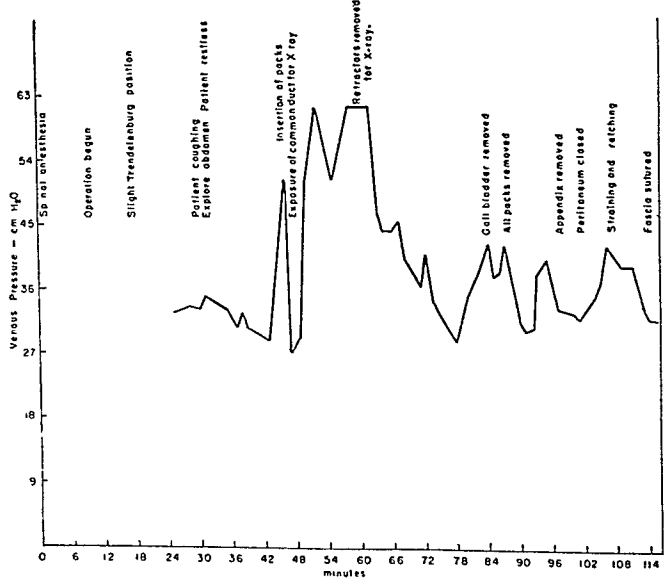


FIGURE 9. Cholecystectomy and Appendectomy (spinal anesthesia).

tending the earlier work of McLachlin¹¹ also showed that stimulation of the end of the cut sciatic nerve produces venous spasm. Franklin and Donegan⁹ and from the present study, it appears that local venospasm is a possible factor in the rise in venous pressure obtained in the course of certain operations. If it is a cause of the increases noted, it is

important to know its duration. The increases obtained in our experiments often continued for thirty minutes or longer. The duration of the rise

in sixty to ninety minutes. This adjustment is probably the result of the opening up of collateral circulation and a general increase in the size of the

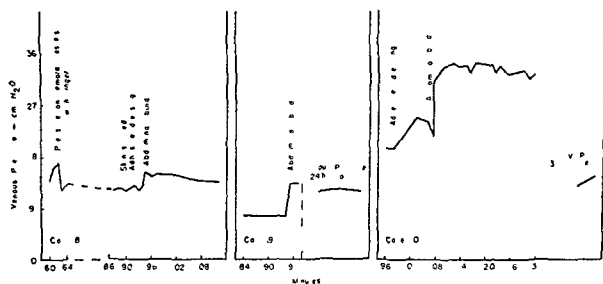


FIGURE 10 Effect of Abdominal Binder after Repair of Unilateral Hernia

cannot be used as an indication of the duration of obstruction due to spasm. Thus, after a ligature is placed around the common iliac vein at its junction

vascular bed. Similar changes undoubtedly occur on obstruction to other vessels, and the slow fall in venous pressure observed in our experiments may

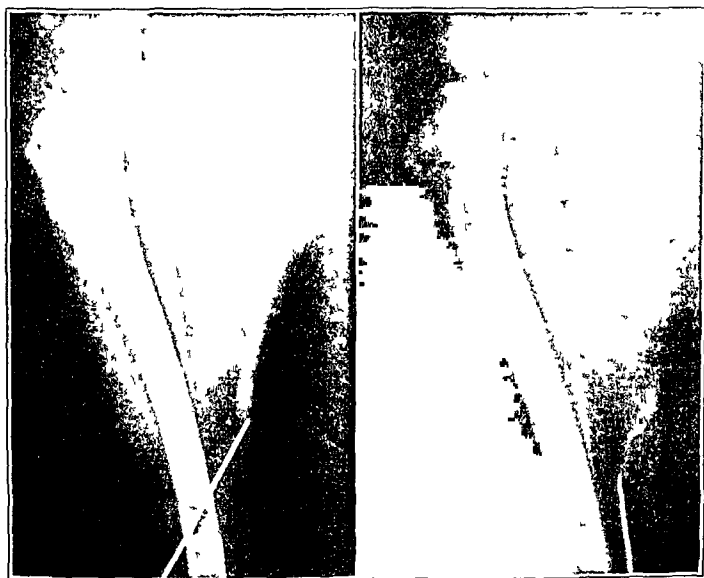


FIGURE 11 Diodrast Venograms before and after Stimulation of the Peripheral Cut End of the Sciatic Nerve in a Dog

tion with the venous cavity in a dog or a cat, the venous pressure in a leg vein rises rapidly to a level of approximately 120 cm of water, after which it falls slowly, reaching the previous normal value¹²

have a similar basis. Thus a normal or only slightly elevated venous pressure at the end of the operation does not exclude the continued operation of factors responsible for the antecedent rises

The rises in venous pressure following the application of a binder after herniorrhaphy are probably best explained by mechanical obstruction to the venous return at the anterior rim of the pelvis. Similar rises are obtained by applying moderate pressure directly over the femoral vein in this region. Whatever the mechanism, the importance of avoiding a tight binder is apparent.

SUMMARY AND CONCLUSIONS

Marked increases in venous pressure were observed in the veins of the foot in the course of operations on the uterus and its adnexa. Less striking changes were noted during cholecystectomy and inguinal herniorrhaphy.

The possible role of local venospasm in the production of these increases is discussed.

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BOSTON MEDICAL LIBRARY

REPORT OF THE PRESIDENT*

THE year 1942, included with the month of December, 1941, the first thirteen months of our participation in World War II, has had the expected and inevitable repercussions on the Boston Medical Library, increasing our expense, diminishing our income, posing new difficulties of administration and interfering seriously with the work of our librarian and our director in maintaining the normal flow and use of medical literature. The Trustees voted to remit the dues of fellows who entered active service with the colors; resignations, presumably owing to difficult economic conditions, increased in number; and thus our income from dues decreased by \$497 as compared with 1941. Income from investments was \$12,984 as compared with \$14,922, a decrease of \$1938, and in spite of rigid economies our operations showed a deficit for the year of \$1305.91. On March 16, 1942, the Trustees voted an increase of 10 per cent in the salaries of our small and devoted staff, to meet at least in part the increased cost of living.

The most unexpected administrative problem that arose during the year was the necessity for meeting the situation created by the sharp limitation of the oil available for our heating plant. The Oil Rationing Board, in December, 1942, announced that they could promise us only enough oil to keep open for one week during each month. It was impossible to change from oil burners to coal-burning grates without a prohibitive expen-

diture, and the problem was solved—I hope successfully—by contracting with the Boston Edison Company to make suitable installations and supply steam for heating. With this assurance of our purpose to co-operate, the Oil Rationing Board promised enough oil to enable us to carry on until the conversion is completed. The cost to us of this installation, the increased cost of heating and a statement of its efficiency will be subjects for the next annual report.

An anniversary of great significance to us was the semicentennial of the entry of our director, Mr. James F. Ballard, into the service of the Library. On October 24, 1892, as a boy of fourteen, he applied for work to Dr. Brigham at the modest little home of the Library on Boylston Place. Beginning then as a stack and errand boy he has served us continuously and efficiently ever since, educating himself in the technic of library administration and acquiring a familiarity with medical literature and a knowledge of medical bibliography that has placed him in the front rank of medical librarians in this country and won him the position of director of the library. The Trustees voted to establish and solicit contributions for the James F. Ballard Publication Fund, with which it is hoped to issue from time to time items that will make better known to its friends the treasures and resources of the Library. In his report as librarian Dr. Viets tells of the proposed publication of the first of these issues, *A Catalogue of Medieval and Renaissance Manuscripts and Incunabula in the Boston Medical Library*.

*Read at the annual meeting of the Boston Medical Library, March 2, 1943

The policy to be pursued in shaping the course of the Library to the end that it shall be increasingly prosperous and useful to the profession, and thus to the public, has continued to receive the earnest consideration of the Trustees. In the annual report for 1941 note was made of a survey, whose cost was defrayed by the Carnegie Corporation, of the resources and inter-relations of the various collections of medical books and periodicals in Boston and its vicinity. It will be recalled without going into details that this report urged that the Library be developed in the future, as in the past, as a reference and research library, supported morally, and if possible financially, by the lesser libraries of medical schools and hospitals, whose working collections would be supplemented by loans and exchanges from our own. During the past year meetings were held by representatives of the Library, of Boston University, Tufts and Harvard medical schools and of various hospitals to discuss the matter, and a substantial agreement of principle was reached without the disclosure of actual ways and means. An informal subcommittee has continued to study the matter. Especially helpful and full of suggestions has been Mr. Keyes D. Metcalf, director of the Library of Harvard University, who, after surveying our building, equipment and collections, was positive in his recommendation that our aim should be to complete our stacks, finish and furnish the periodical reading room, improve the conveniences of Holmes Hall and, last but not least, increase and strengthen our overworked staff. In his opinion the Library could thus be made adequate and convenient for the ensuing twenty-five or thirty years.

What would be the approximate cost? Before the war, the estimated cost of five new tiers of steel stacks was \$70,000; the appropriate finishing and improvements in the periodical reading room and Holmes Hall might require \$15,000, and a capital sum to yield an income of \$10,000 would take care of the enlargement of our staff, of neglected binding and rebinding and of useful development of our services to the community. There are surely farsighted and generous persons who can be helped to see the far-reaching importance of medical library facilities to Boston and New England and who would include us with the hospitals and other charitable institutions that they propose to support by gifts and bequests. A gift may be designated for some special purpose as a memorial or otherwise, or given as a capital sum whose income shall be spent for some indicated purpose or, better still, a gift or bequest may be free of all restrictions, to be used at the discretion of the Trustees. The generous support by New England people of all forms of education is traditional. Is it too much to believe that some of our 800 fellows will be able to convince prospective donors of the privilege that is offered them in bringing to their notice the needs of the Boston Medical Library?

Lest we forget, it should be added that those of us whose imaginations take flight occasionally among the nebulae, still dream of the tax-harassed plutocrat of the future, who may find surcease from his cares in endowing a splendid academy, built about the collections and perpetuating the name of the Library.

DAVID CHEEVER, *President*

REPORT OF THE LIBRARIAN*

IT IS again the privilege of the librarian to bring to the attention of the members of the Boston Medical Library a report on the Library for the year 1942. We have continued along lines similar to those in the past with surprisingly little change in view of the war conditions. Chiefly, we have been forced to curtail some of our services, and the hours of opening have been abbreviated to a marked extent. Toward the close of the year it was necessary to give up opening in the evenings, and finally the Library had to close its doors as early as three o'clock in the afternoon. This was a considerable hardship, for our members were greatly restricted in regard to the time when they could draw books from the Library or visit the building itself. Our visitors,

moreover, were inconvenienced, since many of the students formerly used the Library in the evening. Thus our attendance fell off from the 1941 figure by about 2500, reducing the total number of people who came to the Library to less than 10,000 during the year, a reduction that has not occurred during the previous five-year period.

There was, in consequence of this, a decrease in circulation, but not so much as one might expect. Over 33,000 volumes or pamphlets were taken from the shelves during the course of the year, thus maintaining about the rate of 10 per cent of the total books and pamphlets in the Library that are in use each year. The total holdings at the end of the year were over 325,000 items, there being a gain of about 2500 books. This is our normal rate of increase in recent years, al-

*Read at the annual meeting of the Boston Medical Library, March 2 1943.

though not so large as formerly. The loss, however, is not mainly in books, but in foreign periodicals. The figure in 1940, when we added more than 1500 bound periodicals, can be compared with slightly over 650 in 1942. The chief loss in the periodicals is in the complete absence of French and German journals, which were formerly a considerable part of our yearly gain. To compensate for these, however, we have added a few new American journals, and the English journals are still received in nearly a normal amount. We have added only a few books to the special collections, thus putting most of our emphasis on new books and current periodicals. This, we believe, is in trend with the times, for there is an active interest in all that is new in medicine and to supply this need is the duty of a library such as ours. It is interesting to note, moreover, that our inter-library loans are an increasing part of our service and that we are now supplying, in addition to the ordinary demands from various libraries in New England, the Army and Navy centers as well as important munitions plants. Calls came, for instance, during the year from the General Hospital at Fort Banks in Winthrop, the Fort Devens Service Club, the Lovell General Hospital at Fort Devens and the United States Veterans Administration at Bedford. In addition, books and journals went to the Edgewood Arsenal for the United States War Department, the National Fireworks, Incorporated, and E. I. du Pont de Nemours and Company, Wilmington, Delaware. Thus, it would seem that our library is appreciated both by our members and neighbors, and by those who live some distance from us. We may modestly state, moreover, that we are doing our share in the war effort and supplying those who ask for our services.

A number of events of considerable importance to the Library occurred during 1942. In the autumn, Mr. Ballard, the director, completed fifty years of service to the Library,* and in his honor a reception was held, attended by many of his friends. In addition, he received many congratulatory letters and other evidences of esteem. In writing to the librarian on this occasion, Mr. H. U. Holzer, whose firm, U. Holzer, Incorporated, founded by his father, has bound books for the Library since about 1875, recalls some of the early days when he, as a boy, began to follow in his father's footsteps.

My first recollections of Boylston Place are very strong with me today. I have a very vivid feeling of the old place, the meeting room, which seemed to me

an awesome cave; walls, stairs, landings, rooms, closets, all lined with books, and the heartening presence of Dr. Brigham, who was the most invigorating personality I have ever known. It all blends into an integral part of that time of my life.

In August, 1888, I carried my first load of books from Boylston Place to Bromfield Street, in a small wheelbarrow, inherited from my small-boy predecessor. The whole distance was paved with round cobblestones,—and to a small country boy's self-consciousness, even a small wheelbarrow can seem to fill the air with clatter,—from Cambridge to South Boston.

It did not take long before I learned to transfer the laceration from my pride to my body, by carrying what the wheelbarrow would hold on my shoulder.

By the time Mr. Ballard entered the service, transport was in the hands of my successor, who, being city-bred, was not bothered by the clatter of the wheelbarrow. It was therefore somewhat later that I made Mr. Ballard's acquaintance, and we became James and Henry, and began to travel down the years together.

Presently we were chartering a horse and team for deliveries and pickups, and by 1912 gasoline displaced oats for our transportation. I hope and trust that we may not have to revert to the wheelbarrow.

Fifty years! Sixty years! The length of my definite memory of this city. What they have wrought to Boston Medicine!

In the earliest days my godparents occupied a cottage on Longwood Avenue, exactly where the Richardson House, of the Boston Lying-in Hospital now stands. For a coincidence, Dr. Richardson was the first human to set eyes on me.

Opposite the cottage, from Longwood Avenue to Francis Street and from Huntington Avenue to Vila Street, was an apple orchard, and where the Peter Bent now stands I have played three-o-cat. I suppose Peter at that time was in full cry after the dollars with which to transform that land.

Behind the cottage, as far as Massachusetts Avenue, was only marsh and creek, where we children skated and ran teets when I visited on winter days. Not one of the great assembly of institutions now there existed except in dreams. What about other parts of the city? In the region about Tufts Medical, was, first, a great exhibition building, which burned, a series of animal circus stands and a Fall of Pompeii spectacle, all long since departed.

At the other end of the city, so far as I can remember, the Bulfinch Building contained all there was of the Massachusetts General Hospital. Today there is a medical metropolis round about it.

Dr. Maurice Richardson used to come into the shop and tell my father that he thought there must be some books ready for binding at the Treadwell Library. Father would go down and gather up the periodicals from table and closet, making up complete volumes, and chasing up missing numbers, later sending me down to get them with the accursed wheelbarrow. It seems to me that my father was the only acting librarian. Since then, first Mrs. Myers, then Miss Williams, each have put in years as full-time librarians, and now Miss Lewis is in charge.

In the very first days of my working, there came into the shop a little smiling young lady, with an irresistible manner, asking for dollar contributions for the

*Recognition of the occasion was noted by the *New England Journal of Medicine* (227:610, 1942), the *Journal of the American Medical Association* (120:626, 1942), the *Bulletin of the Medical Library Association* (31 iv, 1943) and others.

Boston Dispensary. Annually, for years, she re-appeared, and on her face we could see the passage of time, as she gathered wrinkles, as well as dollars, until at last she was quite an old lady.

Today, gathered about the little dispensary, which asked for dollar contributions, is the Joseph H. Pratt Hospital, the New England Medical Center Building and I know not what extensions.

What about the Harvard Medical School? Full many a trip did I make to 688 Boylston Street to get books from the professors: Bowditch, Wood, Harrington, Ernst, Councilman and others. Their personal checks paid the bills. They had all made their studies in Germany, and were well disposed toward the Swiss bookbinder, who knew so many languages, and whom they met at the Orpheus Musical Society, where he was active.

Since those days, the great school buildings have arisen, with the professional librarians, the great central library and the various department libraries — all these on that same old apple orchard of my boyhood.

Verily, I shall soon believe that out of little acorns, great oaks do really grow.

Besides this, on every hand, hospitals, and more hospitals, with libraries that appear on our ledger.

As to individual doctors: On how many a sloshy night have I left burdens on their doorsteps! — Bush, Bowditch, Holmes, Hays, Blake, Rotch, Chadwick, Farlow, Minot, Wesselhoeft, Homans, Warren: a host and yet a host.

Secondly, Mr. Ballard has prepared for the Library a catalogue of its medieval manuscripts and incunabula.¹ This has been a congenial task for him, for the collation of these precious books has been one of his prime interests for many years. Beginning with a few books left to the Library by Oliver Wendell Holmes, the Collection has grown through the purchases from the John Warren Fund and the large and valuable collection of incunabula assembled by Dr. William Norton Ballard, to which have been added many more through funds left by Dr. Ballard at the time of his death in 1931. With the manuscripts of Jewish medicine, bought through the Geoffrey M. Hyams Fund, we now have more than 700 manuscripts and incunabula in the Library. It seemed fitting to the Board of Trustees that Mr. Ballard, at this time, should make such a catalogue, and it has been the pleasure of the librarian to assist him in checking some of the items and aiding in the publication. A note from the introduction to the book by the librarian will give the members some idea of the size and importance of this collection.

A general impression of the contents and scope of the collection may be obtained by checking the Catalogue with Klebs's well-known short title list, *Incunabula Scientifica et Medica*. Over one thousand titles and three thousand editions are given by Klebs. Of the various classifications, the largest is medicine, with eight hundred and fifty editions. Of these, this Catalogue lists a rich store, the first and in many cases

other editions of Hippocrates, Galen, Rhazes, Abulcasis, Avicenna, Maimonides, Brunswig and Ketham. In addition, Plato, Averroes, Aristotle, Pliny, Ptolemy, Alfraganus, Albumasar, Rabanus Maurus, Haly Abbas, Guy de Chauliac, Regiomontanus, the *Gart der Gesundheit*, Bagellardus and Gernisonus are well represented. There is a goodly list of the works of Albertus Magnus, a considerable number of almanacs, the writings of Beroaldus, Ficinus and Trithemius, the rare *Lehre und Unterweisung* and a few examples of the *Regimen Salernitanum*. George Sarton, in illustrating his long review of Klebs's *Incunabula Scientifica et Medica*, chose forty-nine books, "to give the reader a fairly good idea of the scientific incunabula." If this is used as a check, first eliminating some of the books in other fields than medicine, thirty-one titles are left to be considered. The Boston Medical Library collection contains, of the thirty-one, twenty first editions and five later editions. Of the remaining six, four are so rare that it is unlikely that copies will ever be available. Thus, the collection is reasonably well rounded out, not lacking in any particular field. The scholar will find some edition in the Library of nearly every book of medical interest published before 1501.

The third event of importance was the restoration of a valuable portrait in the Library. For some years we have owned a portrait of Samuel Danforth (1740-1827), Paul Revere's physician and one of the founders of the Massachusetts Medical Society. In connection with the Revere Exhibit at the Museum of Fine Arts in the fall of 1942, the Danforth portrait was sent to the Museum. There the picture was cleaned and, much to our surprise, it was found to be an exceptional example of the great art of Gilbert Stuart. It is even considered by some as one of the best portraits ever painted by Stuart, and thus the Library contains a rare and exceedingly valuable picture. The trustees of the Museum of Fine Arts gave it an important place in their exhibit, and added publicity came through the publication of a book, *Paul Revere and the World He Lived In*,² by Esther Forbes at about the same time. The portrait is of a man of handsome features, exquisitely delineated by the artist.

In addition to these three important events, the librarian would again call attention to the varied interests of its members. We have to collect on a wide base, for difficult it is to predict what interests the persons who use our library may have. Samuel Eliot Morison,³ for instance, in writing his life of Christopher Columbus, wishing to include a chapter on syphilis,* turned to us for the pertinent material. In addition, during the past year there has been an increased use of our rare books, particularly the manuscripts and incunabula, by scholars both here and from a dis-

* A chapter, "The Sinister Shepherd," in the second volume, contains a description of the disease and its spread among the Indians and the Indian captives.

² *Indian Captives*.

³ *Grand Journal of*

rance. Our own members, too, are beginning to use our library as only a librarian could wish for them to do. Their interests, as I have noted above, are indeed almost as varied as that of the great John Hunter and his wife. Mrs. Hunter was a most charming and accomplished woman who was particularly fond of music. Haydn was one of her close friends and, indeed, she wrote the words for Haydn's great classic, *The Creation*, and for at least a dozen of his songs. John Hunter, however, was interested in Haydn for quite another reason; for Haydn is said to have been the possessor of a particularly fine nasal polyp, and the story goes that Hunter tried to remove this without the owner's consent.⁴

Whether you are interested in the latest research on polyps or, indeed, in music, the Library tries to supply your wants. Only recently there have come to hand two examples of the verse of Oliver Wendell Holmes set to music. One is the rare "Battle of Lexington" and the other the "Ballad of the Oysterman." We have not forgotten, therefore, that someone might be interested in music, and thirty-six pieces by physicians or distinctly medical in character were added to the Library in 1942. We have tried, moreover, to supply the latest information about nasal polyps, and do the best we can to keep up with the times by furnishing you with the current texts and periodicals. For the texts, in large part, we are indebted to the *New England Journal of Medicine* and the reviewers of these books who so generously donate them to our shelves.

Of the special accessions to the Library, I need only mention one or two. To the early printed-book collection we have added an Augsburg almanac for 1470, one of the earliest of its type. A fourth edition of the *Fasciculus Medicinæ* by Ketham completes our collection of this fundamental work. To our American account books we added one kept in the late eighteenth century by Nathaniel Saltonstall of Haverhill, Massachusetts. Our early English imprints, now one of our main interests, have been increased by more than a dozen items.*

*Details of recent accessions will accompany the author's reprints. Copies may be had at the Library.

As usual, we are indebted particularly to our friends, both past and present, for large collections of books and periodicals. From Mrs. Frederick T. Lord was received Dr. Lord's library, and many books have been given by Dr. William C. Quinby, Dr. E. Stanley Abbot, Dr. James L. Gamble and others. Further installments of foreign medical dissertations and theses, in exchange for our public-health items, have been received from the Harvard Medical School. From Dr. Horace Binney, the Library came into possession of the medical chest of Dr. Barnabas Binney, of Philadelphia, a surgeon in the American Revolution. To these donors and others, the Library is indeed grateful.

Most changes in the Library that have been long contemplated have been held in abeyance for the duration of the war. We should not forget, however, our primary aim as an individual institution, namely, that we become the natural repository for books and other items of medical interest in Boston and its vicinity. Moreover, we hope to make closer and firmer, as time goes on, our relations with our sister institutions, in the meantime keeping our status as a distinct part of New England life. To the Boston Medical Library, one should naturally turn first for all books of medical interest. If we should not be the fortunate possessor of some desired book or pamphlet, the staff will make every effort to serve you by procuring this book as rapidly as possible. For failure to serve you quite as completely as we have in the past, we offer no apology. It is too obvious that we also are part of the war effort, and that adjustments must be made to the insistence of the world conflict.

HENRY R. VIETS, *Librarian*

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MEDICAL PROGRESS

ADVANCES IN MALARIA RESEARCH

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BOSTON

MALARIA has been and still is one of the great medical enigmas of the world. The discoveries in the late nineteenth century and in the early years of this century gave great promise of providing the necessary information for the control and eventual eradication of this disease. This utopian achievement has not taken place, and it is now realized that new approaches and methods are needed to control malaria as it exists today, let alone eradicate it. Even the impetus given to malaria research by Wagner-Juaregg¹ in 1917, when he established the value of induced malaria in the treatment of parietic patients, and by the development of the synthetic antimalarial drugs, atabrine in 1933 by Mauss and Mietsch² and plasmochin in 1927 by Schulemann et al.,³ has failed to aid materially in reducing the tremendous yearly toll in morbidity and mortality caused by the disease.

The significance of this fact is well recognized by malariologists, medical entomologists, sanitary engineers and medical officers who have the job of controlling malaria in tropical and subtropical, endemic and hyperendemic malarious areas. Since the troops fighting for the Allied Nations in World War II are scattered throughout the malarious areas of the world, malaria control has assumed an extremely important position in the strategy of the war. Simmons⁴ has reviewed the scope of the problem and has given an account of the comprehensive program placed in operation by the Army to control malaria among our troops. It is quite obvious that the sum total of present knowledge is being utilized and applied in this program to prevent the occurrence of a serious malaria epidemic such as the opposing armies experienced in the Macedonian campaign during World War I.^{5,6} The effectiveness of this campaign has yet to be determined, but it is no idle prediction to state that failure of the program as planned can result only from a lack of basic knowledge and of trained personnel.

A potential malaria problem is facing the country as a whole. In World War I, relatively few of the military forces of the United States were en-

gaged in active service in endemic malarious areas. In this war, however, the majority are or will be engaged in such areas. Troops will come home on leave, will be invalidated home, and will eventually be discharged from the service after having served in malarious areas. Actually this is not only a malaria problem but a problem involving many diseases found in subtropical and tropical climates. Furthermore, this is not only a problem for the future but one for the moment. In New England, there have been cases of malaria among soldiers returning from maneuvers in the South, and a few British and American seamen coming into the port of Boston direct from Africa have had malignant tertian malaria and have been treated here.

Consequently, the purpose of this article is not to present a comprehensive review of malaria research, but to point out those contributions that will help in making a prompt and accurate diagnosis of malaria, to discuss the newer knowledge of pathogenesis and physiology of malaria, to consider the current conception of immunity in malaria, and to review briefly the value of antimalarial drugs for treatment and prophylaxis.

SPECIES OF MALARIAL PARASITES

Malaria is commonly referred to as a single disease entity, but actually four infections produced by four different species of parasite are involved: tertian malaria, caused by *Plasmodium vivax*; malignant tertian (estivo-autumnal or sub-tertian) malaria, caused by *P. falciparum*; quartan malaria, caused by *P. malariae*; and ovale tertian malaria, caused by *P. ovale*. The geographical distribution, incidence and nature of these infections and the morphology and differential diagnosis of the parasites are thoroughly presented in available textbooks and manuals.⁷⁻¹⁴

Benign and malignant tertian malaria are the outstanding and most widespread infections. Quartan malaria, although of importance in Central Africa and parts of India, has a decided tendency to involve certain local and isolated areas. Infections with *P. ovale*, discovered and described in East Africa by Stephens,¹⁵ are very mild and are also rare. There are some doubts about the validity of this species, but the persistence of distinctive morphology after repeated passage

*The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. \$5.00).

¹Instructor in comparative pathology and tropical medicine, Harvard Medical School and Harvard School of Public Health.

through insect and human hosts, together with immunologic and clinical differences,^{16, 17} has helped to establish the species on a firm biological basis.

The use of induced malaria for the treatment of general paralysis of the insane has not only established the therapeutic value of the procedure, but has provided malariologists with an experimental method and host. Clinical malaria may be studied under controlled conditions, and abundant material may be obtained for study both from the human host and from anopheline mosquitoes infected by feeding on patients undergoing treatment.

The most significant advances obtained from the study of induced malaria have to do with the specific validity of the four species of malarial parasites and the discovery of different races or strains of parasites within a given species. The latter discovery has been of great value because it has helped to explain various problems of host susceptibility and immunity. These are discussed below; at this point, it is sufficient to say that these strains can be recognized by their virulence, antigenicity, infectivity for mosquitoes and reaction to quinine and other drugs.

Another source of evidence is the study of avian and simian malaria. Contributions from the laboratory study of avian malaria were stimulated by the discovery of the life cycle of the parasite in *Culex* mosquitoes by Ross, after he had found pigmented cysts on the stomachs of dappled-winged mosquitoes.¹⁸ This type of malaria has also been extremely useful in testing antimalarial drugs. The description of *P. gallinaceum* by Brumpt¹⁹ and its subsequent use by Indian and American workers for studies in immunology have opened a new approach to the subject. The simian parasites, *P. cynomologi*, *P. inui* and *P. knowlesi*, have also been used experimentally with profit. The discovery of *P. knowlesi* in *Silenus irus* by Sinton and Mulligan²⁰ has greatly aided the advance of knowledge. When this parasite is inoculated into the rhesus monkey (*Macaca mulatta*), an infection develops that, if untreated, usually ends fatally in six to ten days after onset. The particular attribute of this species and also of *P. gallinaceum* is the high percentage of parasitized cells that develop during the later stages of infection (*P. knowlesi* 30 to 75 per cent, *P. gallinaceum* 30 to 80 per cent). Thus, for the first time heavy concentrations of parasites may be obtained for physiologic and immunologic studies.

LABORATORY DIAGNOSIS

Morphologic Diagnosis

When one recalls the great variety of clinical symptoms produced by cases of malaria, the vari-

ous atypical states of infection and the absence of symptoms in latent malaria, it becomes clear why a diagnosis of malaria is entirely dependent on finding and identifying the parasites in the blood. Through lack of facilities and of a proper technic and skill in detecting the plasmodia in blood films, the general practitioner and clinician too often neglect this essential procedure.

The current laboratory methods of preparing thin and thick films and of staining them satisfactorily have become simplified enough to be mastered by anyone with some facility and experience in microscopical technic.¹³ The practitioner should at least know how to prepare satisfactory films for shipment to a state laboratory or to a medical school for examination, if the procedures and examination cannot be performed in the private laboratory.

The technic of preparing thin blood films and staining them with the Romanowsky stains (Wright's, Leishman's or Giemsa's) is commonly known. Repeated studies have shown that the thick-film technic is advantageous for the discovery of a lower concentration of parasites and for saving time in performing the examination.¹³ The thick-film method is one of concentration. A large drop of blood is placed on a thoroughly clean slide. With the corner of another slide, a needle or other instrument, the drop is spread so that the red corpuscles are several layers thick in the center, tapering off to a single layer at the margin. The film should dry flat, and when it is dry one should be able to read print or see the hands of a watch through its thickest part. Before staining, the film should be placed in an incubator at 37° C. for one hour or kept at room temperature overnight.²¹ It should not be heated or flamed, because the cells will thus be fixed and dehemoglobinization of the red cells will be prevented. The film should be stained within forty-eight hours because of degenerative changes that take place in the drop, preventing differentiation in staining.

Dehemoglobinization of the red cells and staining of the parasites is carried out simultaneously in a 2 per cent Giemsa solution for forty-five minutes, or in a 10 per cent Wright-Giemsa solution for ten minutes.²² American-made (National Aniline and Chemical Company) Giemsa and Wright's stain can be used to make the required stock solutions. Only neutral or buffered water should be employed for diluting the stock stain, in order to ensure uniform results and also to prevent precipitation of the dye. Preparation of the buffered water can be carried out by the method of Field and Le Fleming²³ or that of Wilcox and Logan.²⁴

Field and Le Fleming's method Dissolve 0.5 gm of anhydrous disodium phosphate (Na_2HPO_4) and 0.4 gm of potassium acid phosphate (KH_2PO_4) in 1000 cc of distilled water (if $\text{Na}_2\text{HPO}_4 \cdot \text{H}_2\text{O}$ or $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ is used the quantity must be recalculated). This solution should have a pH of 7.0-7.2. If a different pH is desired the quantities of the salts are varied according to standard sodium buffer standards.

Wilcox and Logan's method M/15 Na_2HPO_4 (95 gm of the anhydrous salt per liter) and M/15 $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$ (92 gm per liter) or M/15 KH_2PO_4 (90 gm per liter) are mixed in the following amount: the final volume being made 1000 cc by the addition of distilled water. pH 7.0-6.1 cc of the former and 38 cc of the latter, pH 7.2, 72.0 cc of the former and 28.0 cc of the latter.

Wright-Giemsa stain¹³ Dissolve 2 gm of Giemsa powder in 100 cc chemically pure glycerin from a freshly opened bottle with the aid of heating in a water bath at 55 to 60°C for two hours. Precaution must be taken to avoid absorption of moisture during the process particularly when the mixture is stirred. To this solution add 100 cc of aged Wright's staining solution (2 gm of Wright's stain in 1000 cc of chemically pure methyl alcohol). Let stand overnight then add 800 cc of aged Wright's staining solution. Filter.

A thorough knowledge of the morphology of malarial parasites must be acquired before attempting to make a microscopic diagnosis. The stained thin film is the method of choice for studying the typical morphologic characteristics of malarial parasites, and for the novice this is the best method for differential diagnosis. Nevertheless, the thick film technic is preferable for the reasons already given. Experience in thick film examination is necessary, however, before one can make a reliable diagnosis from it. Since from ten to fifty times more blood can be examined on a thick film than on a thin film in a given amount of time, the method should be mastered and utilized by all workers called on to make frequent or occasional blood examinations for malarial parasites.

A differential diagnosis of species should be established in all cases of malaria. A patient with malignant tertian malaria obviously requires more careful handling and treatment than does one with benign tertian infection. Finally, information concerning the previous use of antimalarial drugs should be obtained from each patient at the time blood is taken for examination. These drugs lead to the quick destruction and developmental inhibition of the parasites in the peripheral blood and may result in failure to find the parasites. Whenever there is any doubt and whenever possible, successive blood films should be taken at suitable intervals during at least two or three days to determine the existence of infection and to arrive at the correct differential diagnosis.

Serologic Tests

Since both chronic and latent malaria often exist without detectable parasites in the peripheral blood serologic tests is supplementary diagnostic procedures have held out a great deal of promise. Efforts to devise successful tests were greatly handicapped by the inadequacy of antigens prepared from infected human blood which has a relatively low density of parasitized cells.

The availability of several species of simian parasites particularly *P. knowlesi*, led to the following significant studies on the immunology of malaria. In 1935, Coggeshall and Eaton¹⁴ were able to demonstrate complement fixing antibodies in rhesus monkeys with a chronic *P. knowlesi* infection, using *P. knowlesi* antigen. Later Eaton and Coggeshall¹⁵ used the same test to study serums from human infections with *P. knowlesi* and with *P. vivax* and *P. falciparum*. Strong complement fixation was obtained with the three types of serum. Thus the reaction was shown to be a group reaction rather than a specific one.

This test has now been applied by Dulaney and Stratman-Thomas¹⁶ and Kligler and Yoeli¹⁷ to test serums from human cases of malaria in an effort to determine the value of the procedure for practical diagnostic purposes. In a later paper, Dulaney, Stratman-Thomas and Warr¹⁸ have shown that the test is highly specific for malaria, and again that it is group specific. They report 102 positive reactions (82 per cent) with serums from 125 patients who had demonstrable malarial parasites in their blood at the time serum was taken, 15 positive reactions (9 per cent) of 192 presumably malarious patients with negative blood films, and 24 positive reactions (14 per cent) in a group of 170 presumably nonmalarious patients who were suffering from bacterial or other protozoan diseases. Serums from syphilitic patients with no malaria gave no higher percentage of nonspecific malarial reactions than did normal serums.¹⁹ Kligler and Yoeli¹⁷ examined 309 serums obtained in a hyperendemic area, with 98 per cent positive reactions in children under twelve years and infected adults. Healthy adults gave 10 per cent positive reactions. Kligler and Yoeli also showed that serums of persons given repeated treatment react according to the interval between the last attack and the date of onset. Dulaney and Stratman-Thomas have pointed out that early treatment inhibits the development of complement fixing antibodies. The test appears to have practical use for epidemiologic purposes¹⁹ but the reaction is more valuable as a supplementary test than as a substitute for the examination of blood films.²⁰

In 1938, Eaton³⁰ demonstrated the presence of agglutinins in serums from monkeys with a chronic infection of *P. knowlesi*. Within the limits of the work, the agglutination reaction was specific, giving positive results only when a homologous combination was used. The observation that normal red cells and cells with immature parasites did not agglutinate in antiserum offers a basis for explaining the slow humoral response in antibody production and the activation of the lymphoid-macrophage system for cellular defense in the host. Because of the low density of parasites in human malarial infections, no similar tests have been performed with human malarial parasites and immune serums.

An important series of contributions was initiated in 1940 by Mulligan and Russell³¹ when they demonstrated the specific agglutination of sporozoites of *P. galinaceum* by dissecting salivary glands of infected mosquitoes in homologous antiserum in dilutions as high as 1:8000. Mulligan, Russell and Mohan,³² working with sporozoites and immune serums from human, fowl and sparrow malaria, presented strong evidence for the specificity of the reaction. Sporozoites of human malaria were agglutinated in a titer of 1:4000 by serums from chronic human cases. Sporozoites of sparrow malaria, *P. praecox*, were agglutinated in the extraordinary high titer of 1:8000 to 1:65,000 when chronic homologous serum was used. Cross-agglutination was observed in some cases to a titer of 1:128, indicating a slight group reaction. Although the method has possibilities for application to the diagnosis of human malaria, practical difficulties in providing and maintaining a supply of infected mosquitoes will no doubt prevent its adoption.

A precipitin test was devised by Taliaferro and Taliaferro³³ in 1928 in which an extract of human placenta from a case of malaria was used. This work has not been applied practically because of the scarcity of infected placentas for making the required antigen. The majority of workers with simian malaria have failed to get positive results. Dulaney and House³⁴ have been able to obtain a precipitative reaction with an antigen from *P. knowlesi*. Both the collodion-agglutination method of Cannon and Marshall³⁵ and the collodion-fixation procedure of Goodner³⁶ gave positive results. Macroscopic agglutination was obtained by both precipitative methods.

Skin tests have been devised for malaria, but the results do not seem to be consistent or significant. Hermann and Lifschitz³⁷ worked with human malaria, and Sinton and Mulligan³⁸ with monkey malaria. Stratman-Thomas and Dulaney³⁹ failed to repeat the above positive results and

stated that the reactions obtained did not fulfill the criteria for a delayed type of intradermal reaction.

Chemical Tests

Although the ferro-flocculation and melano-flocculation tests of Henry^{40, 41} were claimed to be specific antibody-antigen reactions, extensive studies have shown that this is not the case. The positive results obtained with serums from cases of malaria are dependent on an altered ratio of serum proteins. For this same reason positive tests were obtained by numerous other workers in a wide variety of diseases, such as typhus, kala azar and Weil's disease.^{42, 43} The pigments acted as indicators and not as antigens.

With the explanation available for the mechanism involved in Henry's reaction, Proske and Watson⁴⁴ developed a protein-tyrosin reaction to make a quantitative chemical estimate of the amount of euglobulin present in the serum from patients with malaria. The test is no more specific than Henry's reaction, but is much simpler. The reaction and results have been confirmed by at least one group of workers.⁴⁵

PATHIOGENESIS

No generalization can be made about the course and severity of malarial infection without qualifications regarding the kind of malaria involved, the area in which the disease was contracted, and whether the malaria was naturally acquired or induced. It is true that tertian and quartan malaria have more constant courses than has malignant tertian malaria, which is very variable in its clinical manifestations.

The human malarial parasites are generally considered as well-defined species, but actually, as shown below, there are definite morphologic and physiologic differences between strains of the same species obtained from different malarious areas.

Objections may be raised to comparing the basic observations that were made with naturally acquired and induced malaria, since the latter is usually produced in paretic patients by the direct inoculation of infected blood from patient to patient. These objections have been met in many laboratories by using infected mosquitoes to induce the disease.

In a typical case of tertian or quartan malaria, the basic clinical symptoms of rigor, heat and sweating during a certain time of the periodic cycle are associated with the cyclical development of the parasites in the blood. The beginning and duration of the paroxysm are correlated with the rupture of the parasitized red cells and the setting free of the new crop of merozoites into the

plasma. The original observations of the associated phenomena were made by Golgi,⁴⁶ but the periodic phenomena for *P. malariae* have now been worked out in greater detail.⁴⁷ The growth of trophozoites took 54.2 hours, young schizonts 10.4 hours, and segmenters 7.4 hours, six of which were required for segmentation. The progress of segmentation was closely followed by a rise in temperature until the process was completed. A different time schedule exists in tertian and malignant tertian malaria, but the relation of the shorter paroxysm to the segmentation of the parasites is apparently the same.

The underlying phenomena causing the paroxysm are not understood. Many theories have been offered, but few facts are known. The release of the merozoites and the pigment and constituents of the ruptured red cells provides a sudden increase in protein that may cause the phenomenon. The latter is believed to be similar in some respects to an anaphylactic reaction.⁴⁸ Even though one reads in the literature about toxic substances and the increased toxicity of epidemic malaria, no concrete evidence is as yet available for the secretion and liberation of such toxic substances. Other authors⁴⁹ believe that the rise in the plasma potassium level may be responsible for the sequence of events. Beeson and Hoagland⁵⁰ found that intravenous injections of calcium chloride (10 cc. of a 10 per cent solution) stopped the rigor almost immediately.

Recent studies with the pigment (hematin) of *P. knowlesi* have identified this substance spectroscopically as ferrihemic acid.^{51, 52} The same workers tried to demonstrate the role of the pigment in the production of the paroxysm⁵³ and the lesions.⁵⁴ No evidence of a causal relation between pigment and toxicity was obtained. Toxic symptoms developed only when the reticuloendothelial system was overwhelmed by the accumulation of parasites. Furthermore, the pigment at the time of liberation from the ruptured cell was found to be insoluble in the plasma.

The observations just cited leave the cause of the paroxysm still undiscovered. In fact, the mechanisms involved in the production of the paroxysm and symptoms are still more baffling when one considers the symptomless carrier, and when one compares the numbers of parasites per cubic millimeter of blood at the onset of symptoms and for varying intervals after spontaneous cure. Usually the parasites are present in much greater numbers at the time the symptoms disappear. This phenomenon and also the relapse are no doubt related to the immune response as well as to the inherent pathogenesis of the disease.

The pathogenicity of human plasmodia differs between species and between strains of the same species. Primarily, the parasites gain entrance into the blood stream after a variable incubation period and invade the red corpuscles, where they multiply asexually and also differentiate into gametocytes. The destruction of red cells on the completion of each new asexual cycle leads to anemia, which is correlated in intensity with the severity and duration of the disease. The cellular detritus, pigment, merozoites that fail to penetrate new cells and old gametocytes are taken up by phagocytes. Since the volume of material for phagocytosis varies with the intensity of the infection, the quantity is great enough in most cases to cause a proliferation of the reticuloendothelial system. For this reason, the parasites localize in the spleen, liver and bone marrow to produce hypertrophy, hyperplasia and pigmentation.

In malignant tertian malaria, the parasitized red cells may localize in any organ because of their tendency to agglutinate spontaneously and to adhere to the walls of the small capillaries. Thrombi are then formed, leading to stasis of the blood supply and occlusion of the capillaries. Cannon⁵⁵ in an outstanding discussion of the pathology of human malaria presents a case to confirm the spontaneous agglutination of parasitized red cells. Knisely et al.⁵⁶ have demonstrated the phenomenon in vivo, using a color moving-picture film to record the sequence of events in the blood of a rhesus monkey injected with *P. knowlesi*. Rigdon⁵⁷ failed to find evidence of spontaneous agglutination in a patient dying of uncomplicated malignant tertian malaria and autopsied three hours after death. This author suggested that shock resulting from anoxemia is worth considering as the cause of death in infection with *P. falciparum*. In any case, the blocking of capillaries by parasitized red cells helps to explain the great variety of symptoms in pernicious malaria, and the sequence of events is responsible for the types known as "cerebral" and "algid." Cannon presents excellent evidence for the similarity between the courses of malarial and of bacterial infection, a fact that is not generally recognized by malariologists.

The parasites of tertian and quartan malaria are not so invasive as is *P. falciparum*, and the counts per cubic millimeter do not approach the 300,000 to 500,000 seen occasionally in fulminating cases of pernicious malaria. The density of *P. vivax* is seldom greater than 100,000, and *P. malariae* seldom exceeds a density of 20,000. Even though the parasitic densities in quartan infection are extremely low, the paroxysms are usually very severe.

Valuable information concerning malaria in drug addicts has been obtained by clinical and

laboratory studies. The method of infection depends on the direct transmission of the parasites by the use of common hypodermic syringes. Biggam⁵⁸ first reported this type of infection among drug addicts in Cairo, Egypt, in 1929, and the first report in this country was made in 1932.⁵⁹ Additional papers from other workers in this and other countries followed within a short time. Helpern⁶⁰ presented a study of 49 cases in New York City, 29 of which were fatal. Most⁶¹ has studied over 200 cases, all except 2 of which were malignant tertian malaria. These papers deserve attention, particularly by physicians on the staffs of large city hospitals, who are more likely than others to be confronted with this type of patient. A high percentage of cases are brought into hospitals in a comatose condition because of cerebral involvement with *P. falciparum*. Early diagnosis by the demonstration of malaria parasites in the blood is necessary, this to be followed by prompt and intensive treatment in order to prevent fatalities, which even then are very high.

Most pointed out that the malignant tertian malaria seen in his series of cases differed in no way from naturally acquired infections in the tropics. Cerebral syndromes were the most frequent, but gastrointestinal or algid types were seen, along with 2 cases of hemoglobinuria or blackwater fever, 1 of which was fatal.

The course of the disease and its pathology, as studied by Helpern and by Most, were characteristic of malignant tertian malaria. Death in the majority of cases was attributed to the overwhelming infection and diffuse cerebral involvement. No observations were included that add to those made by Cannon⁵⁵ on the intravascular agglutination of parasitized cells, although photographs were shown to demonstrate the filling and occlusion of small capillaries.

PHYSIOLOGY

The physiologic pathology of malaria has been reviewed by Meloney,⁶² who concludes a summary of this extensive subject by saying, "There are few infectious diseases of man which, in their severe manifestations, produce functional changes in more regions and systems of the body than malaria." Consequently, the variety of clinical symptoms caused by malaria are more understandable when the physiologic changes taking place in this infection are realized.

Of interest are recent studies⁶³⁻⁶⁵ on induced malaria made in an effort to find the cause for the edema commonly seen in parietic patients undergoing treatment. These observations demonstrated a reduction of the plasma proteins, especially that of albumin⁶⁵ and have led Kopp and

Solomon⁶⁴ to the conclusion that the edema is the result of reduced osmotic pressure caused by a marked fall of the albumin fraction to levels of 3 gm. per 100 cc. or below. The most important factor in determining this drop in the synthesis of albumin is the interference with its production in the liver. The destruction of red cells by the parasites accounts in part for the increase of globulin. A period of twenty-four days was required after the termination of the attack before the blood proteins returned to their normal values.

The physiology of the malarial parasites is not clearly understood because of the same difficulties that have hampered studies on humoral immunity. No adequate methods of cultivating these parasites are known, and they generally occur in a relatively low concentration in the peripheral blood during the human disease. The discovery of the simian parasite *P. knowlesi*,²⁰ which produces over 50 per cent infected red cells in the rhesus monkey, has provided a rich source of organisms for studies of metabolism and immunity. With improved methods devised during these studies, species causing less intense infections are also being investigated.

Dextrose was found to be essential for the limited survival of human plasmodia according to the technic of Bass and Johns.⁶⁶ Christophers and Fulton⁶⁷ and Fulton⁶⁸ showed that glucose causes an increase of oxygen consumption by *P. knowlesi*. Coggeshall⁶⁹ showed that *P. knowlesi* consumes six times as much oxygen as does *P. inui*. Maier and Coggeshall,⁷⁰ improving the methods of Christophers and Fulton, found that the oxygen uptake is proportional to the size or developmental stage of the organism, and that glucose appears to meet the normal energy requirements of the parasite. Application of the studies on respiration was made by Fulton and Christophers⁷¹ in order to test the effect of quinine and atabrine on the parasite in vitro. Coggeshall and Maier⁷² went one step farther and investigated the possibility of assaying antimalarial drugs by their effects on respiration and comparing the results with their therapeutic action. The in vitro method could not be used to furnish a reliable chemotherapeutic index, but had value as a supplementary test along with in vivo experiments.

The precise role of diet in racial and individual susceptibility to human malaria is not understood. The great influence that famine exerts on the intensity of epidemic malaria in India has long been noted.⁷³ However, the epidemics usually followed a period of famine, indicating that lack of proper food was a predisposing cause. Passmore and Sommerville⁷⁴ have pointed out that the association of malnutrition and malaria does not

prove that malnutrition is an essential factor in the causation of epidemics. In fact, these authors reviewed the conflicting views of various authors and in particular those of Sinton⁷⁵ who has pointed out that malaria may be the direct cause of poverty and an insufficient diet. The numerous factors involved in the general picture of adverse economic conditions are difficult to study and assess in the field.

Avitaminosis and its general effect on resistance to infection may play a part in making a community highly susceptible to an outbreak of epidemic malaria, but experimental evidence is lacking. The degree of immunity existent in the population is also a factor, because low transmission at a time of drought allows the immunity to fall to a low level in the older age groups, and is not sufficient to produce immunity in young children if they are not exposed to infection. Consequently, the complexity of factors involved in endemic and epidemic malaria has prevented accurate analyses of the part played by malnutrition and dietary deficiencies. The coincident and repeated conduct of a thorough nutrition survey in conjunction with the malaria survey in a highly malarious area over a period of years would provide invaluable medical and public-health data.

Clinical investigations by Lotze⁷⁶ showed that greater quantities of vitamin C than normal were utilized by patients with benign tertian malaria, and the vitamin was found to play a part in salt and iron metabolism. Mohr⁷⁷ confirmed these findings and insisted that no causal relation exists between malaria and avitaminosis C; the administration of additional vitamin C, he stated, aids convalescence from malarial anemia by enhancing the value of iron.

Passmore and Sommerville,⁷⁴ working with simian malaria and diets deficient in vitamins A and C and calcium, failed to demonstrate differences in primary infections between a well-nourished and a poorly nourished group of monkeys. Actually, the average parasite counts were higher in the well-nourished group. This finding at least confirms the observation that a good state of nutrition does not reduce the severity of primary attacks of malaria in human beings.

The relation of biotin to susceptibility to avian malaria has recently been studied by Trager.⁷⁸ When ducks and chickens on a deficient biotin diet were injected with *P. lophurae*, 50 to 100 per cent heavier infections developed. The parasite count remained high several days longer and the mortality was greater than among the controls. At the peak of the malarial infection, the concentration of biotin in the blood reached two to three times its normal value, a fact that Trager points

out may well be concerned with the elimination of the parasites from the blood stream. The application of these results to similar studies on human and simian malaria should provide some interesting and highly valuable data.

(To be concluded)

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**BENJAMIN CASTLEMAN, M.D., *Acting Editor*EDITH E. PARRIS, *Assistant Editor*

CASE 29321

PRESENTATION OF CASE

A fifty-one-year-old unmarried woman, a stenographer, entered the hospital because of "generalized weakness."

Approximately one month prior to admission the patient noticed increasing difficulty in climbing stairs because of "weakness in the knees." Two weeks before admission her ankles began to swell, particularly in the evening, and at times her face was slightly swollen. Weakness gradually became generalized, and she felt extremely fatigued each evening. Her physician noticed that her voice had become quite deep, acne had developed on the face, hair had grown on her upper lip and chin, and her eyebrows had become bushy. She had gained 3 pounds in the previous month. During the two years prior to admission she had occasionally suffered with bitemporal headaches, often associated with palpitation. There had been no dyspnea, cyanosis or angina.

The family history was noncontributory. Twenty-six years prior to admission, a panhysterectomy, right oophorectomy and partial left oophorectomy were done for ovarian cysts and endometriosis. Menses ceased after this operation but no hot flashes occurred.

Physical examination revealed a large woman, weighing 175 pounds, who talked in a rather husky tone. The eyebrows were bushy. Hair was prominent on the upper lip and to a less extent on the chin. The hair on the head was not remarkable. The fundi were normal. There were crusted and pustular lesions on the face and between the breasts. The cheeks were fat. The subcutaneous fat seemed abundant on the trunk, upper arms and thighs. The skin was rather flushed; several small striae were present over the iliac crests. Both breasts were small. The heart, lungs and abdomen were normal. Vision was 20/20 in the right eye and 20/25 in the left eye. The visual fields and blind spots were normal. There were many fine and deep varices of the legs and thighs. Pelvic

examination revealed an absence of organs or masses. One examiner believed the clitoris was slightly enlarged. The tendon reflexes were sluggish. Muscular weakness was generalized but more evident in the lower extremities. No muscular twitches were noted, and there was no muscle tenderness. Sensations to pinprick and light touch were normal. The position and vibration senses were reduced in the legs, but the plantar reflexes were normal.

The blood pressure was 220 systolic, 106 diastolic. The temperature was 99.2°F., the pulse 84, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,860,000 and a white-cell count of 10,300, with 89 per cent neutrophils. The urine was alkaline and had a specific gravity of 1.012; the sediment contained 2 white cells per high-power field and a great deal of amorphous material, and the urine gave a "green with slight precipitate" test for sugar. A blood Hinton test was negative. The fasting blood sugar was 127 mg. per 100 cc., and the nonprotein nitrogen 20 mg. The chloride was 92.0 milliequiv. per liter. The prothrombin time was 23 seconds (normal, 19 seconds). The total protein was 4.8 gm., the albumin 3.1 mg., the globulin 1.7 mg., the calcium 9.6 mg., and the phosphorus 3.1 mg. per 100 cc. Another fasting blood sugar before a glucose tolerance test was 156 mg. per 100 cc., and the test levels were 262 mg., 282 mg., 300 mg. and 360 mg. in one half, one, two and three hours respectively. There was no sugar in the urine specimens collected during the test. A phenolsulfonephthalein test showed 45 per cent excretion, 15 per cent in the first fifteen minutes. The fasting blood sugar before an insulin tolerance test was 136 mg. per 100 cc.; the test levels were 115 mg., 94 mg., 85 mg., 91 mg., 111 mg. and 123 mg. at twenty, thirty, forty-five, sixty, ninety and one hundred and twenty minutes after the intravenous injection of 7.9 units of insulin. Adrenalin (0.79 cc. of a 1:1000 solution) was then administered, and forty-five and sixty minutes later the blood sugar levels were 162 mg. and 145 mg. per 100 cc. respectively. In three examinations the 17-ketosteroids were 16.8 mg., 10.4 mg. and 10.2 mg. in twenty-four-hour urine specimens. The urine contained less than 6.6 mouse units of follicle-stimulating hormone per twenty-four-hour urine specimen. The basal metabolic rate was +15, +7 and -1 per cent in three satisfactory determinations.

An electrocardiogram revealed a normal sinus rhythm of 70. The PR interval was 0.14 second. There was high voltage in the standard leads. The QRS complex was 0.09 to 0.10 second. Q₁ was 11 mm., and Q₄ 1 mm. There was evidence of

*On leave of absence.

moderate left-axis deviation. T₁ was upright, and T₂ inverted. There was slight sagging of the ST segment in Lead 2. The T wave was inverted in Lead 3, and there was late inversion of the T wave in Lead 4. The spinal fluid was normal.

A chest roentgenogram was negative except for a linear scar in the left lower lung field. The heart was transverse in position, and the aorta tortuous. X-ray examination of the skull showed a normal sella turcica. There was considerable increased density along the suture between the squamous portion of the temporal bone and the parietal bone. The squamous portion of the temporal bone was thin. A lateral view of the thoracic spine showed moderate osteoporosis. There was no evidence of vertebral fracture. The kidneys appeared normal in size, shape and position. There was an irregular area of calcification low in the pelvis. Intravenously injected dye appeared promptly in both kidneys. There was incomplete visualization of the calyces and pelves owing to overlying bowel content. The ureters appeared normal. The area of calcification was partially obscured by the bladder shadow. A barium enema was negative except for several diverticula in the sigmoid. There was no definite evidence of extrinsic pressure on the bowel.

The patient was treated symptomatically and discharged unimproved on the twenty-third hospital day. Her diabetes was controlled by diet without insulin. On the day of discharge the chloride was 78.5 milliequiv. per liter, and the nonprotein nitrogen 23 mg. and the sugar 162 mg. per 100 cc.

Final admission (five weeks later). The patient re-entered the hospital because of increased generalized muscular weakness and dryness of the mouth.

The patient looked apathetic, but seemed quite comfortable. Scattered fine and medium moist rales were audible at the lung bases posteriorly. The heart and abdomen were normal. There was slight pitting edema at the sacrum and increased weakness of the hands and back. The muscles of the hands, calves and thighs were atrophied, but no fibrillations were seen. The tendon reflexes were sluggish, although there was marked reduction in vibration sense and in two-point discrimination in the lower extremities. Pinprick was felt less acutely on the legs than on the trunk and upper extremities, although the soles of the feet were very sensitive. Perception of light touch seemed normal.

The blood pressure was 135 systolic, 90 diastolic. The temperature, pulse and respirations were normal.

The red-cell count was 3,850,000, and the white-cell count 9600, with 93 per cent neutrophils. The urine was neutral in reaction, had a specific gravity of 1.015 and gave a ++ test for albumin and an olive-green test for sugar. The sediment contained 25 white cells per high-power field and a great deal of amorphous debris. The creatine and the creatinine urinary excretions were 360 mg. and 512 mg., respectively, in twenty-four hours. The blood nonprotein nitrogen was 28 mg. per 100 cc. and the sugar 244 mg.; the carbon dioxide combining power was 37.3 millimols per liter. The vital capacity was 30 per cent of normal. In a flat plate of the abdomen the left kidney was lower than usual. There was a shadow somewhat suggestive of a mass above the kidney, but this was not definite.

A biopsy of a leg muscle was done. The surgeon commented on the difficulty in finding any muscle tissue. The sections showed degenerative changes in the muscle fibers, as evidenced by a marked increase in sarcolemma nuclei. There was some increase in fat and connective tissue.

The blood sugar remained high despite 20 units of regular insulin and 20 to 30 units of protamine zinc insulin daily, but the urine was freed from sugar by the insulin. Two weeks after admission the carbon dioxide combining power was 34.4 millimols, the chloride 84.5 milliequiv. and the sodium 140.8 milliequiv. per liter. The protein was 3.8 gm., the albumin 2.4 gm. and the globulin 1.4 gm. per 100 cc. The pH of the blood was 7.39. The urine at that time was alkaline and gave a + test for albumin; it showed a ++++ test for chloride in the twenty-four-hour specimen. The sediment contained 6 white cells per high-power field, amorphous debris and many bacteria.

The patient was treated with testosterone propionate. Since the urinary output was 940 cc. per day, ammonium chloride was administered, producing a marked diuresis. Approximately one month after admission petechial hemorrhages were noted in the skin of the abdomen, particularly in an abdominal scar, and of the chest. The prothrombin time was 28 seconds (normal, 20 seconds). The sugar was 235 mg., the protein 4.2 gm., the calcium 8.7 mg., and the phosphorus 13 mg. per 100 cc. The carbon dioxide combining power was 35.1 millimols per liter; the chloride was 83.9 milliequiv., the potassium 3.18 milliequiv. and the sodium 133.9 milliequiv. per liter. The pH of the blood was 7.7. The total 17-ketosteroid excretion was 11.8 mg. every twenty-four hours (alpha type 8.4 mg., and beta type 3.4 mg.). The urine was negative for 3 mouse units of follicle-stimulating hormone, per twenty-four-hour speci-

men. A perirenal air injection disclosed a smooth mass, measuring 9 by 6 by 0.5 cm., overlying the superior pole of the left kidney at the level of the eleventh and twelfth ribs. There was considerable air in the fascial planes and probably within the abdomen. Twenty-four hours after the injection there was a large amount of mediastinal emphysema and subacute emphysema in the neck. The patient gradually became drowsy and uncooperative, and increasing edema developed in spite of the administration of Mercupurine.

On the thirty-third hospital day Cheyne-Stokes breathing developed, the blood pressure dropped in spite of transfusions and coramine, and the patient lapsed into coma and died.

DIFFERENTIAL DIAGNOSIS

DR. MAURICE FREMONT-SMITH: This fifty-one-year-old stenographer complained of generalized weakness and swelling of the ankles for a month before admission. She had acne of the face, and hair on the lips and chin; the eyebrows had become bushy, and her voice deep.

I think the best way to discuss this case is to "jump in" on the question of Cushing's disease, because the symptoms of weakness, slight masculinization, hirsutism, high blood pressure and diabetes, make a discussion of this disease inevitable.

Cushing's syndrome is usually, if not always, associated with hyperplasia or cancer of the cortical cells of the adrenal gland and frequently with certain changes in the basophilic cells of the pituitary gland. Cushing found basophilic adenomas in many of his cases, but such adenomas have not always been found in this syndrome,* and their significance is still not clear.

One thinks of the adrenal gland as the primary etiologic factor in Cushing's syndrome, and there are a number of factors here that favor this syndrome. I should mention particularly two things: the type of the diabetes, and the very low amount of follicle-stimulating hormone in the urine. A low excretion of follicle-stimulating hormone can be present with destruction of the pituitary gland (as in panhypopituitarism) and also following suppression of pituitary activity by estrin producing tumors (arrhenoblastomas). We must remember the possibility of the latter in this case, because although most of her pelvic organs were removed at an earlier age for endometriosis, part of one ovary was left and arrhenoblastoma was therefore still possible.

The type of diabetes here, the insulin-resistant variety, is found in Cushing's syndrome. Protein

is rapidly turned into sugar; and this not only leads to too much sugar (diabetes) but to too little protein (accounting for the weakness). There is no absence of insulin in this condition; hence, the administration of insulin produces slight, if any, lowering of the blood sugar and does not make up for the defect. This patient had marked insulin resistance. In the insulin-tolerance test, in thirty minutes after the injection of a proper amount of insulin, the blood sugar should be about half the fasting level. Here the thirty-minute level was well over half the fasting level. Moreover, insulin given to this patient did not control the diabetes.

In Cushing's syndrome there is also a slight increase in the excretion of 17-ketosteroids. Such an increase was present in this case. The acne is typical. The blood pressure is characteristic. But when one comes to the further laboratory data and the subsequent course one's hope for Cushing's syndrome is greatly upset. In the first place this patient was running a constant alkalosis and had a very low serum protein. The alkalosis I think could be explained by the loss of chloride. The urine contained a large amount of chloride, and the blood chloride, even in the first examination, was extremely low. If a person is losing chloride without losing base, alkalosis will certainly result. The patient was not vomiting. Why she was not losing base, I do not know. I hope I shall get help from someone here. The low serum chloride is one of the characteristic changes that take place in Addison's disease, but in Addison's disease sodium is also lost, and potassium retained. Consequently we are faced with what looks like hyperactivity of certain cortical cells on the one hand (Cushing's syndrome) and loss of activity of the cortical cells on the other.

DR. TRACY B. MALLORY: Do you not mean medullary cells?

DR. FREMONT-SMITH: No; I mean cortical cells. As I said, some factors here suggest overactivity of the cortical cells, others underactivity. I think that can possibly be explained by the fact that in Cushing's syndrome the androgenic cells are the overactive cells.† In a case reported by Wilkins,¹ there was hyperplasia of the adrenal androgenic tissues and death resulted from corticoadrenal insufficiency. I wish to see whether I can fit this case into a similar type of lesion.

Let us run through the vast amount of laboratory work here. The chlorides were low, and the nonprotein nitrogen was normal, which is against Addison's disease. The low total protein probably accounted for the edema. Low total protein is

*The term "Cushing's syndrome" is used when speaking of the clinical picture without regard to the etiology. The term "Cushing's disease" is reserved for those cases with basophilic adenoma of the pituitary gland.

†This is a misstatement. M. F. S.

not found in Addison's disease because the body loses water, together with the electrolytes, and hemoconcentration results. The calcium was 9.6 mg., and the phosphorus 3.1 mg. I should not make any reference to the calcium, even in the presence of the low serum protein, if it were not for the fact that later on, when the calcium was lower (8.7 mg.), the phosphorus was 1.3 mg. That is probably a red herring, but if you will remember that in determining the serum calcium you must add 1 mg. to the calcium reading for every milligram the total protein falls below 7 mg., you will see here that by adding 3 mg. to the calcium value one is left with a figure of 11 mg.; this and a phosphorus level of 1.3 mg. are consistent with hyperparathyroidism. I only raise that as an interesting speculation and will ask Dr. Albright to say a word about it. The renal function was somewhat low, — 15 per cent in the first fifteen minutes, — but it does not seem that the kidney function was badly damaged.

The ketosteroids were high for a woman who is as sick as this woman was. Normally the alpha type represents 90 to 95 per cent of the total ketosteroids. I am tempted to make a diagnosis of cancer of the adrenal cortex on the basis of the high percentage of beta ketosteroids reported here. But in all the cases of adrenal cancer about which I have heard the total excretion of ketosteroids is extremely high, ranging from 50 to 100 mg. in twenty-four hours. In my diagnosis I shall be influenced more by the comparatively low ketosteroid excretion than by the disproportion of the alpha and beta steroids. I shall therefore make a diagnosis of hyperplasia rather than cancer of certain cells of the adrenal cortex, with consequent pressure on the cortical cells that secrete the anti-Addison's disease hormones. I may be absolutely wrong, but I make it on the basis of the absence of a great increase in excretion of total ketosteroids.

Running through the other facts here, I think the electrocardiogram shows coronary heart disease, but not coronary thrombosis. This, again, is consistent with Cushing's syndrome, which is often accompanied by coronary disease. The absence of x-ray evidence of tuberculosis in the chest makes Addison's disease unlikely, since about 80 per cent of Addison's disease is the result of tuberculosis. There was not, as there often is in Cushing's syndrome, a high red-cell count. I should also mention the creatine output, which was extremely high in this case. The normal woman puts out little creatine, and this large output is consistent with Addison's disease, as well as with hyperthyroidism and myasthenia gravis. The creatinine output was low, which is consistent with the paucity of muscle tissue ob-

served by the surgeon. The biopsy of the leg muscle I shall not discuss.

The only other important thing is the finding by perirenal air injection of a tumor above the left kidney. May we see the x-ray films?

DR. LAURENCE ROBBINS: This skull film shows a sella that is normal in size and shape with perhaps slight decalcification of the vault. The bones of the spine are decalcified, and in this film we are able to see that the left kidney is considerably low in position and that there is a suggestion of a mass above it. Although these films were taken after an air injection, unfortunately the air did not choose the right pathway to help us out. It failed to outline the kidney and adrenal gland as well as it often does, but there is a mass lying in this area above the kidney that is outlined by the air in part, and I can say that, in spite of the normal upper pole of the kidney, which can be seen in the lateral view, there is something lying above it. This chest film was taken rather late in the disease and simply shows atelectasis and the decalcification of the bones, which have been seen elsewhere. I do not see anything to suggest active tuberculosis. Possibly some of these areas of density represent old areas of calcification.

DR. FREMONT-SMITH: I have not explained the low serum protein, except possibly by inanition. I shall make a diagnosis of hyperplasia of certain groups of cells of the adrenal cortex, with pressure on the other parts of the cortex and resultant destruction and Addison's disease; and in the pituitary gland I expect to see nothing except the changes in the Crooke cells that may go with Cushing's syndrome. There may be hyperplasia of the parathyroid glands. I believe there will be no lesion in the pancreas or ovary. There will also be the changes that go with hypertension; some arteriosclerosis, coronary heart disease and sclerosis of the kidneys.

DR. FULLER ALBRIGHT: I am afraid that I have been guilty of spreading misinformation. We did at one time think that all cases of cancer of the adrenal gland had a very high 17-ketosteroid excretion. This was true of our first 3 cases; however, some of our other cases had normal or only slightly elevated values. They had a case of cancer of the adrenal gland with Cushing's syndrome and normal ketosteroid excretion at the Mount Sinai Hospital in New York City. Concerning beta ketosteroids, when they are high it probably means cancer; when they are low, however, it does not mean that it is not cancer. Their excretion was not high in this case, in spite of the fact that, as Dr. Fremont-Smith has stated, their percentile

value with regard to total 17-ketosteroid excretion was increased.

The low serum phosphorus was probably the result of giving testosterone. When testosterone is administered, new tissue is formed and that takes a lot of phosphorus.

There are so many things to talk about that it is difficult to choose the significant points.

A PHYSICIAN: Did the patient have edema?

DR ALBRIGHT: Yes; marked edema.

Let us talk about electrolytes. If she had Cushing's syndrome, presumably she had too much of some adrenocortical hormone. So in the electrolytes one might expect the opposite picture of that seen in Addison's disease. In Addison's disease, there is a low sodium, a low chloride, a normal carbon dioxide combining power and a high potassium. This patient had a normal sodium, a low chloride, a high carbon dioxide combining power and a low potassium. In other words, the findings were not typical of those observed in Addison's disease, with the exception of the chloride. Dr. Fremont-Smith says that she was losing chloride through the urine without base. The urine was alkaline so there was base of some kind with the chloride. It is clear that the high carbon dioxide combining power was compensatory to the low chloride, but otherwise I cannot put the electrolyte picture together. Dr. Edwin Kepler² of the Mayo Clinic has had 3 patients with Cushing's syndrome who had exactly the same alterations in their blood electrolytes. In these cases there was the same tendency to hemorrhage that this patient showed hemorrhage into the subcutaneous tissue. Dr. Kepler's cases all showed hyperplasia of the adrenal glands.

DR FREMONT-SMITH: What was the argument for treating with testosterone?

DR ALBRIGHT: We know that in Cushing's syndrome the patient is suffering from lack of tissue—no muscle, no bony matrix, thin skin and so forth. Testosterone is the hormone par excellence that makes everything grow. This is a type of symptomatic treatment that works well in certain cases. I think Dr. Fremont-Smith's conclusions that this patient was suffering from overfunction of certain functions of the adrenal glands and underfunction of others come very close to explaining the facts.

CLINICAL DIAGNOSES

Cushing's syndrome
Carcinoma of adrenal cortex

DR. FREMONT-SMITH'S DIAGNOSES

Hyperplasia of the adrenocortical cells.
Addison's disease?
Hypertensive heart disease.

ANATOMICAL DIAGNOSES

Adenocarcinoma of left adrenal gland, with metastases to the liver, lung and bronchial lymph nodes

Atrophy of right adrenal gland.

Central necrosis of liver.

Pulmonary edema, moderate.

Hydrothorax, bilateral.

Cardiac hypertrophy, hypertensive type

Peripheral edema, moderate.

Hirsutism.

Atrophy of skin and muscles

Operation perirenal air injection, left.

Mediastinal emphysema.

PATHOLOGICAL DISCUSSION

DR MALLORY: The post-mortem examination answers some of the questions, but many others are unanswered.

The primary finding was a large tumor, weighing 180 gm., in the left adrenal gland. This was cortical in type. It was a malignant tumor and had caused a large metastasis to the right lobe of the liver and also small metastases in the lungs and bronchial lymph nodes. One of the interesting findings was the size of the right adrenal gland, which showed extreme atrophy, weighing only 18 gm. One adrenal gland was completely replaced by tumor, and the other extremely atrophic. I think that that probably explains fairly well this queer combination of evidence of hyperactivity and subactivity of the adrenal cortex at the same time.

We were limited by the autopsy permission to an abdominal incision, so I cannot tell you about the parathyroid or pituitary glands. We were unable to find any recognizable trace of ovary. There certainly could not have been any ovarian tumor. The heart showed moderate hypertrophy and slight coronary disease. The lungs showed a moderate amount of emphysema. The one other finding that may have been influenced by some of the metabolic conditions was a rather severe extensive central necrosis of the liver. It is not possible to say how long it had existed. I think it was probably a matter of only a few days before death, but perhaps the final hemorrhages can be explained that way. I doubt if it was of long enough duration to have caused the consistently low serum protein.

DR ALBRIGHT: How about the muscles?

DR MALLORY: They were extremely atrophic.

DR ALBRIGHT: No scar tissue?

DR MALLORY: No.

DR FREMONT-SMITH: Do you think the air injection was the cause of death?

DR. MALLORY: I do not believe so. Several days had intervened. There was detectable emphysema in the mediastinum at the time of autopsy, but that had nothing to do with the patient's death.

DR. ALBRIGHT: How about the smooth muscle in the adrenal glands?

DR. MALLORY: I looked at that with interest but could not make out anything wrong with it.

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CASE 29322

PRESENTATION OF CASE

First admission. A twenty-seven-year-old woman entered the hospital complaining of chest pain.

The patient had felt perfectly well until one and a half years before admission, when suddenly a severe pain developed in the chest immediately to the left of the sternum at the level of the third interspace. It was an aching pain that occasionally radiated to the left neck and was aggravated by deep breathing, sneezing and coughing. At night it was severest, and frequently awakened the patient. The attack lasted only two or three days, but during the ensuing months there was an occasional mild ache in the same location.

One evening five months before admission the severe pain returned, and in the morning, numbness had developed in the left chest and arm and the patient found that she was unable to move the trunk, left arm or head. Her physician could detect nothing abnormal on physical examination, but suggested an x-ray film of the chest; this advice was not followed. Within the next few days the pain and numbness dwindled, and at the end of a week the patient returned to her work as a stenographer. During the next three weeks a dry cough came and went, and in the fourth week the pain disappeared completely. Three months later the symptoms recurred, and the patient began to suffer from anorexia, nervousness and fatigue, and weight loss became perceptible. Again the pain disappeared within a few days, but returned in its severest form one month before admission. Its characteristics were always the same, but in addition it was aggravated by lying on the left side and was eased somewhat by resting on the opposite side. Three weeks before admission a chest plate taken at an outside institution showed a definite abnormality in the left chest. A week later the patient contracted a sore throat

and head cold, accompanied by dull pain in the left side of the chest. She went to bed. Her temperature was normal each morning but rose to 99.2°F. each afternoon. During the next few weeks a dry cough developed but discomfort was experienced only on deep breathing. At no time had there been hoarseness, sputum, hemoptysis or night sweats. A loss of 12 pounds had occurred in the previous four months.

At the age of two the patient had suffered from influenza complicated by pneumonia. In the next year a swelling developed in the left side of the neck; this finally ruptured and drained. Her tonsils and adenoids had been removed when she was seven years old. In general the patient contracted three colds a year, which usually were accompanied by a sore throat and lasted two or three weeks. Her father had died of rheumatic heart disease at the age of twenty-six.

On examination the patient was well developed and somewhat emaciated but in no apparent distress. An 8-cm. vertical scar was present on the left side of the neck, starting just below the ear. The tonsils and uvula were absent. The chest was symmetrical, with a questionable lag on the left. At the level of the second and third ribs on the left side and extending from the midline laterally for 6 cm. there were slight percussion dullness, increased tactile fremitus and slightly decreased breath sounds. The dullness blended with the cardiac area below. There was some doubt about these abnormalities for they could not be detected by other examiners with any consistency. Examination of the heart, abdomen and nervous system was normal.

The blood pressure was 120 systolic, 74 diastolic. The temperature swung between 98 and 100.5°F., the pulse averaged 90, and the respirations were normal.

Examination of the urine was negative. The blood showed a red-cell count of 4,500,000, with a hemoglobin of 13.5 gm., and a white-cell count varying between 7000 and 14,000, with 75 per cent neutrophils. The blood Hinton test and examination of the stools were negative. No tubercle bacilli could be found in the gastric washings. The tuberculin test in a dilution of 1:10,000 was negative, but in a dilution of 1:1000 there was a 2-cm. area of erythema in thirty-six hours that increased to 3 cm. in forty-eight hours, with a 2-cm. ring of induration.

X-ray films of the chest showed a 6-by-5-cm. oval mass with flamelike excrescences at the left hilus, and a lateral film placed it in front of the hilus. The hilar shadows themselves seemed normal in size, shape and position, and the lungs were otherwise clear. The chest films taken three weeks

before in another institution were said to have shown a fairly smooth-bordered triangular mass, 5 cm. wide, extending out from the left hilus. An intravenous pyelogram revealed nothing abnormal.

During hospitalization the patient received 1800 r of x-ray therapy front and back, directed

DIFFERENTIAL DIAGNOSIS

DR. HELEN PITTMAN: Have we the x-ray films?

DR. MILFORD SCHULZ: This is the film (Fig. 1) taken at the first admission. It is somewhat overexposed but shows the triangular area of density arising in the left hilus. The ribs are intact

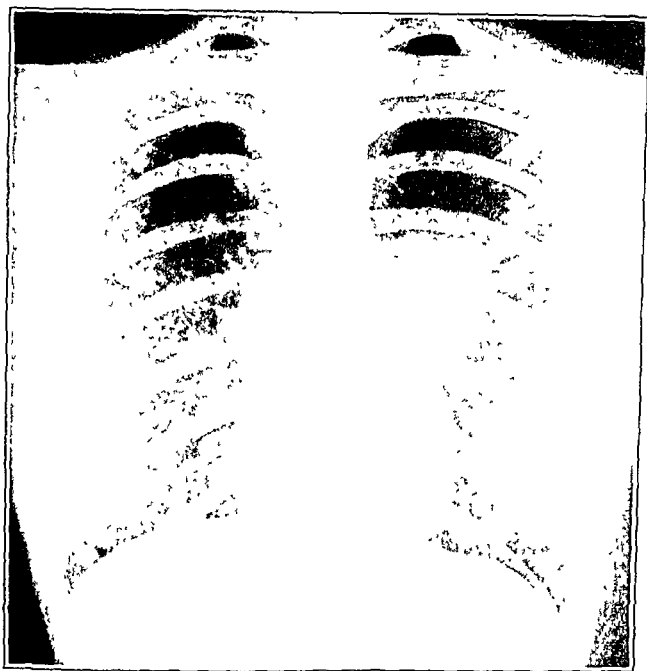


FIGURE 1. Roentgenogram of Chest.

toward the left hilus, over a seven day period. Two days later she was discharged to the Out Patient Department.

Second admission (three weeks later). In the interval the patient remained in bed except for visits to the Out Patient Department. Her temperature had varied between 99.6 and 101.0°F., and she was always aware of pain, although it was not sharp unless she took a deep breath, sneezed, lay on the left side or sat straight up.

A chest film taken two weeks after completion of the x-ray therapy showed that the lesion had not responded; indeed, the examiner believed it to be somewhat larger.

On the tenth hospital day an operation was performed.

and there is no fluid in the chest. The next film was taken after she had received 1800 r, and the lesion, if anything, is larger than in the one taken before radiation. In the lateral film the lesion is at the base of the upper lobe and extends almost to the anterior chest wall.

DR. PITTMAN: Do you think it arises in the mediastinum?

DR. SCHULZ: No; I think it arises in the hilus.

DR. PITTMAN: From the record alone, before seeing the x-ray films, I thought that the lesion was mediastinal. I shall have to change my ideas.

This is a story of sudden onset followed by acute attacks with remissions of one and a half year's duration in a twenty-seven-year-old woman. There is a definitely positive tuberculin test, which

I am inclined to accept as a fact but not to relate to the present lesion. I think that a positive tuberculin test in a dilution of 1:1000 in a twenty-seven-year-old person occurs often enough so that we cannot put too much faith in its having anything to do with this lesion.

Going back to the childhood of this patient, the influenza, the pneumonia and the swelling in the neck are closed episodes. I do not believe they had anything to do with the present illness.

There are queer neurologic findings. Five months before admission the pain in the chest returned with numbness of the left chest and arms and the patient was unable to move the trunk, left arm or leg. This was probably not due to neurologic disease. I think she had pain and was unable to use them for that reason. There is no other evidence suggesting involvement of the nervous system.

Then we come to the time of admission, when the patient was running a low-grade fever, with slight leukocytosis, a positive tuberculin test, chest pain, and very questionable physical findings, which I think are reasonably consistent with the x-ray films. At no time did she have hoarseness, sputum or hemoptysis. She had lost 12 pounds in the previous four months, and it is stated that more than a year ago the patient began to lose her appetite. Whether she lost her appetite from this process, whether it was enough of a process to make her lose weight or whether she lost weight merely because she lost her appetite, I cannot say.

What are the things that could cause a lesion of this sort in the chest? We think of infections, and of course we think first of tuberculosis. I am disregarding tuberculosis as being of probable importance here. She had signs that are consistent with an infection, but I think it was secondary to the process in the lung—whatever it is. The first time she noticed any fever was shortly before she came into the hospital, when it went to 99°F., and in the hospital it rose to 100.5, which is not convincing. She had a leukocytosis, which is consistent with infection. The fact that the pain came and went is not helpful, because what evidence we have does not show that the lesion became larger, and it does not appear to be the kind of lesion in which recurrent episodes of bleeding cause pain from pressure.

Finally we come to new growth, which deserves serious consideration. It is quite obvious that that is what they were looking for when the patient was on the ward. They were thinking of metastasis from a hypernephroma, I assume, when they did a pyelogram. Then the question of lymphoma

probably arose. She was, however, given much more than a lymphoma dose of radiation. Eighteen hundred roentgens is more than enough to knock out a lymphoma or any of that group, although Dr. Holmes told me yesterday that there have been one or two lymphosarcomas that have remained unchanged with that degree of radiation.

If this was in the lung root, which I believe it was, we have to think seriously of carcinoma. I can recall only one case of primary bronchiogenic carcinoma in which the bronchus was so completely occluded that there was at no time any sputum or bleeding. That was in a patient whose first symptoms were those of a mediastinal syndrome from pressure, but that is certainly extremely rare. The lesion is a little too far out to have been a dermoid cyst, which was my diagnosis when I came in. I shall drop that idea and say that it was a new growth that was infiltrating outward, was increasing in size and had survived 1800 r without shrinkage. Therefore, despite the fact that at no time had there been sputum or bleeding, I think that the most reasonable diagnosis, in view of these films, is bronchiogenic carcinoma.

DR. WILLIAM B. BREED: Now that Dr. Pittman has committed herself, I should like to ask Dr. Schulz if he will examine these films again and explain why the original diagnosis by the X-ray Department was lymphoma.

DR. SCHULZ: I know the answer, but I did not know it when I saw these films. Undoubtedly, the flame-like appearance extending into the left lung was Dr. Schatzki's reason for raising the question of lymphoma and for suggesting that a therapeutic trial of radiation be given. These flaring extensions of infiltration into the lung substance are seen every now and then in lymphoma. When it did not respond to radiation, a malignant lesion primary in the bronchus was considered. One member of the department was rather firmly convinced that it was inflammatory.

DR. BENJAMIN CASTLEMAN: Dr. Adams, would you like to comment?

DR. RALPH ADAMS: I think that the lesion was not a carcinoma but was tuberculous in origin and that it can be classified under the general heading of tuberculoma. Tuberculoma, strictly speaking, is thought of as a circumscribed lesion without bronchial communication and without spillage of tubercle bacilli. However, there is another type of tuberculous lesion, to which it is hard to give a one-word name, that fills all the requirements of tuberculoma except that it is incompletely localized or encapsulated. In the x-ray film there seems to be some parenchymal involvement beyond the

mass itself. If I had been discussing the case I think I should have concluded with a diagnosis of tuberculoma, qualifying this term as not strictly meeting all the requirements for accurate pathological description of the lesion.

DR. BREED: I saw this patient two days after she came into the hospital. We then had the re-

as second." After that I confirmed Dr. Pittman's finding that there were crepitant rales above the heart, but I heard none toward the axilla.

DR. CASTLEMAN: Dr. Sweet, will you tell us of your operative findings?

DR. RICHARD SWEET: My first knowledge of this patient was when I wandered into the X-ray De-



FIGURE 2. Photograph of a Cross Section of the Lung.

port of the X-ray Department; also the house-officers had reported dullness above the heart extending out toward the axilla, which I was unable to find. Dr. Pittman, this is the patient whom I asked you to examine without knowing about the case, and you may remember that you found some rales above the heart.

DR. PITTMAN: I do, Dr. Breed.

DR. BREED: On April 12 I wrote as follows: "Unprejudiced by knowledge of previous x-ray findings or physical examinations, I find absolutely nothing abnormal in general and in particular with relation to the chest. X-ray interpretation: lymphoma. From the history I should be inclined to put tuberculosis as first choice, and lymphoma

partment one morning and they asked me to look at these plates, which were on the illuminator. Without knowing anything about the patient I said, "This is a carcinoma," which was a rash statement. Then I heard the story about lymphoma and the lymphoma dosage. We went into the matter further, and I said, "Whatever it is, the patient should be operated on."

There were two things—the sex and the age—against the diagnosis of carcinoma. But, even in the absence of bloody sputum, we still entertained that diagnosis. I did not believe it was a tuberculoma because it did not have the x-ray appearance of those that we have observed in this hospital. Even at operation it looked exactly like a neo-

plastic infiltration of the lung—it had a nodular puckered appearance on the surface and was adherent to some of the pericardial fat tabs. I was convinced that I was removing a carcinoma.

CLINICAL DIAGNOSIS

Carcinoma of lung.

DR. PITTMAN'S DIAGNOSIS

Bronchiogenic carcinoma.

ANATOMICAL DIAGNOSIS

Tuberculoma of lung.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The external surface of the lesion did present a dimpled, depressed, firm area with small subpleural nodules, such as are seen in carcinoma. A cross section of the lung (Fig. 2) showed a 5-by-3-cm. lesion that was pyramidal shaped and composed of numerous round foci of caseation. There was a very dense band surrounding most of the lesion but in some areas the process had spread in an irregular fashion to blend with the surrounding parenchyma. We found no communication with the large bronchi, but a

few of the small branches of the apical bronchus ran through the lesion. Microscopically, the tubercles were active and were separated from each other by broad bands of fibrous tissue. I suppose tuberculoma is the best name for a lesion of this kind, even though it was not completely encapsulated. One regional lymph node also showed caseous tuberculosis.

DR. SWEET: This case reminds me a great deal of certain conditions in the colon. Not long ago two cases with annular constricting lesions in the right colon were discussed in which the diagnosis before and at the time of operation was carcinoma. In both cases the lesion turned out to be tuberculosis. The surgeon under such circumstances is undecided whether to remove the lesion or not. Thinking that in this case the mass was a carcinoma, I went ahead and did a total pneumonectomy. She made a good recovery and went home four weeks after operation.

DR. CASTLEMAN: So far as the operation is concerned, I believe that the treatment was excellent. Although thoracic surgeons are now performing more lobectomies and pneumonectomies for tuberculosis, with good results, in the past tuberculomas were usually resected under the mistaken diagnosis of lung tumor.

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MALARIA

A CONSERVATIVE estimate of men from Massachusetts who have gone into the armed forces is approximately 250,000. These men have been dispersed to camps and schools in this country and to widely scattered outside areas, ranging from Iceland and Alaska to numerous tropical countries and including the fighting fronts in Africa and the South Pacific. A sizable number of these men are now in endemic and even hyperendemic malarious localities, and a certain percentage will contract malaria. The treatment of malaria in the field and at base hospitals is seldom adequate and radical cures are difficult to obtain, leading to the

development of chronic or latent malaria, which persists for varying lengths of time. Tertian malaria (*Plasmodium vivax*) can persist for about three years, malignant tertian (estivo-autumnal) malaria (*P. falciparum*) for approximately one year, and quartan malaria (*P. malariae*) for as long as six or seven years, after which the infections apparently disappear spontaneously.¹ That these figures need revision is shown by occasional references in the literature to the persistence of quartan parasites in adults for as long as thirty years.^{2 3} A latent infection is usually detected in the recipient of a blood transfusion when the donor harbored the infection unknowingly. Thus, with the ability of malarial parasites to persist for varying lengths of time, one can expect to see malaria frequently in troops returning from this war. In World War I this problem did not develop because the troops fought mainly in nonendemic areas.

In a recent report, the Medical Department of the Pan American Airways⁴ states that 46 of 284 men in Africa experienced acute attacks of malaria in spite of the fact that they were taking prophylactic doses of quinine. In an unprotected group, 87 cases of malaria developed in 100 men within five months. Furthermore, Coggeshall⁵ writes that malaria reaches epidemic proportions in combat areas where control is difficult, and that it has been estimated that over 85 per cent of the men of each regiment at the fall of Bataan had acute malaria. Information such as this gives one an inkling of what to expect in returning troops.

Fortunately there is every evidence that the medical personnel is being well prepared and equipped to deal with malaria.⁶ Likewise, it is the duty of physicians responsible for health on the home front to become acquainted with the pertinent newer knowledge about accurate diagnosis and treatment of clinical malaria.⁷ All cases of malaria, military and civilian, should be reported to local and state health officials. If the cases occur during the summer months, and hence the breeding time for anopheline mosquitoes, persons with malaria and patients undergoing treat-

ment should sleep in adequately screened rooms to prevent transmission. Finally, the patient's blood should be examined for parasites from time to time, to be certain that a radical cure has been effected, since relapsing cases are also a source of parasites for transmission.

The QAP treatment (quinine, atabrine and plasmochin), which is the method of choice for treating acute malaria,^{8,9} will be restated in the report on medical progress beginning in this issue of the *Journal*. Few physicians outside the large cities will have access to all these drugs, but quinine or atabrine therapy should be sufficient for the majority of cases. The plasmochin has been included in the combined treatment because this drug specifically affects the gametocytes of *P. falciparum*, thus preventing the transmission and also lowering the relapse rate of pernicious malaria.¹⁰ Quinine or atabrine is active against the asexual stages of *P. falciparum* but fails entirely to devitalize the gametocytes. Obviously, if malignant tertian malaria occurs in a patient who will not be exposed to anopheline mosquitoes, the use of plasmochin is not essential.

A patient with chronic malaria is usually more difficult to cure than one with a primary case. Before a course of treatment is given, such patients should be allowed to go through a certain number of paroxysms to acquire some immunity against the infection.¹¹ This procedure is dangerous, however, with infections due to the highly invasive *P. falciparum*, unless the patient's blood can be examined daily to determine the number of parasites present and hence start treatment whenever multiplication begins to reach a dangerous level. Nevertheless, acquired immunity aids in securing a radical cure and should be utilized whenever possible in treating refractory cases.

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PREVENTION OF SHOCK IN BURNS

THE recent trend in the prevention and treatment of shock resulting from injuries and burns has been to rely almost entirely on plasma transfusions. This procedure has behind it a considerable body of experimental data in animals, as well as a good deal of experience in clinical cases, and also seems to have a sound physiologic basis.

The early use of physiologic saline solution for the maintenance of blood volume in an attempt to prevent early deaths from shock was frequently resorted to in the past but has now been almost completely abandoned. It is even considered by many workers to be dangerous. A recent report indicating that saline solution when properly used may be superior to plasma is, therefore, of considerable interest and may result in a revision of some of the current concepts on this subject.

In a series of carefully controlled experiments, using standardized burns in mice, Rosenthal,¹ a pharmacologist in the Division of Chemotherapy of the National Institute of Health, has studied the effects of various types of systemic treatment on the immediate mortality from the burns. The procedure resulted in burns that were regularly fatal to the mice within forty-eight hours. He observed no benefit from the administration of substances designed to maintain or increase the blood pressure. These included epinephrine, posterior pituitary extract, adrenocortical extract and desoxycorticosterone acetate. All these substances were given subcutaneously following the burns.

Sodium chloride given by mouth or intraperitoneally caused a significant reduction in the mor-

ality. Intravenous administration was less effective, and an isotonic solution given by mouth was superior to hypertonic solutions. Potassium chloride, on the other hand, caused acceleration in the time of death, and when administered together with sodium chloride, it seemed to antagonize the effects of the latter. Calcium gluconate given orally was without effect. An isotonic glucose solution given by mouth showed only slight therapeutic action, whereas the administration of hypertonic glucose solutions or of water by mouth caused the animals to die sooner than the controls. A number of other sodium salts, including the acetate, succinate, bicarbonate and lactate, were found to be just as effective as sodium chloride. Of particular interest is the finding that mouse serum given intravenously was somewhat less active than equivalent volumes of physiologic saline solution given orally. Little effect was observed from the intravenous administration of hypertonic human serum albumin.

These experiments indicated to Rosenthal that the acute mortality following burns in mice is closely related to disturbances in the sodium-potassium balance in the body, as well as to the escape of fluids from the circulation. The former seems to be more important and may be casually connected with hemoconcentration and with the other effects usually ascribed to the loss of fluids in the burned area. This supports the view maintained by Scudder^{2,3} on the role of potassium as a toxic factor in shock, although his ideas are not generally accepted.

Certainly these findings are worthy of careful consideration. If similar results are obtained in large experimental animals, the application of these procedures to the treatment of patients seems warranted. If they prove to be of value in saving the lives of patients suffering from shock, this would result in the saving of large amounts of human plasma that are now used for this purpose.

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MEDICAL EPONYM

BEARD'S DISEASE

A paper entitled "Neurasthenia or Nervous Exhaustion" was read before the New York Medical Journal Association by George Miller Beard (1839-1883), lecturer on nervous diseases at the University of New York. This paper was published in the *Boston Medical and Surgical Journal* (80: 217-221, 1869) and is quoted as follows:

The morbid condition of state expressed by this term has long been recognized, but the special name *neurasthenia* is now, I believe, for the first time presented to the profession.

... I have for some time been in the habit of employing the term *neurasthenia* to express the morbid state that is commonly indicated by the indefinite phrase nervous exhaustion.

The derivation of the term *neurasthenia* is sufficiently obvious. It comes from the Greek *neur*, and *asthenia* being literally interpreted signifies want of strength in the nerve.

... In regard to the pathology of *neurasthenia* we are compelled, in the absence of definite knowledge, to reason from logical probability.

My own view is that the central nervous system becomes dephosphorized, or, perhaps, loses some what of its solid constituents; probably also undergoes slight, undetectable, morbid changes in its chemical structure, and, as a consequence, becomes more or less impoverished in the quantity and quality of its nervous force.

... Among the special exciting causes of *neurasthenia* may be mentioned the pressures of bereavement, business and family cares, parturition and abortion, sexual excesses, and the abuse of stimulants and narcotics, and civilized starvation, such as is sometimes observed even among the wealthy orders of society, and sudden retirement from business.

R. W. B.

RESOLUTION ON THE DEATH OF EDWARD JOSEPH LEONARD

Dr. Edward J. Leonard, late visiting physician on the Medical Service of Carney Hospital, died on February 14, 1943, in his forty-second year, after an illness of many months. Dr. Leonard was born in Boston and was graduated from Georgetown College in 1922 and from Georgetown Medical School in 1926. He served his internship at Mercy Hospital, Baltimore. Shortly after completing his internship he was appointed to the Out-Patient Department of Carney Hospital as physician to the out-patients and later was advanced to visiting physician to the House Staff.

Salmonella infections were reported from: Boston, 1; Haverhill, 1; Holyoke, 1; Medford, 1; total, 4.

Septic sore throat was reported from: Boston, 6; Marion, 1; Wakefield, 1; Williamstown, 1; total, 9.

Tetanus was reported from: Brockton, 1; total, 1.

Trichinosis was reported from: Boston, 1; total, 1.

Typhoid fever was reported from: Boston, 1; Brockton, 1; Chelmsford, 1; Haverhill, 2; Norwood, 1; Quincy, 1; Winthrop, 1; total, 8.

Undulant fever was reported from: Adams, 1; Dartmouth, 1; Hopkinton, 2; Ipswich, 1; Rockport, 1; total, 6.

CORRESPONDENCE

A PHENOL SOLUTION FOR THE TREATMENT OF TRICHOPHYTOSIS ("ATHLETE'S FOOT")

To the Editor: About one and a half years ago, Francis (J. A. M. A. 117:1973, 1941) advocated the use of a mixture of phenol and camphor for the treatment of "athlete's foot." He warned that the mixture was caustic when applied to wet surfaces, and subsequent statements by others have indicated that it is too caustic for general use. After having been frequently afflicted with typical "athlete's foot" for many years, I concocted in 1930 a solution, also containing phenol, that has proved not only completely effective in combating this infection but also harmless even when applied to wet skin. The formula is as follows:

Phenol crystals (melted)	2 cc.
Ethyl alcohol (95 per cent)	2 cc.
Glycerin	4 cc.

The solution is applied by thoroughly rubbing the affected region with the end of a finger kept wet with the solution. The application is usually made twice daily, night and morning. In mild cases one application daily, or even less often, has sufficed. It can safely be made, and is probably most effective, immediately after the feet and lesions have been washed with soap and water. Itching is almost at once overcome by the first application. After the lesion has healed, an application once a week should be continued. Otherwise, in my own case, the condition recurs, sometimes within a few weeks. This may be because of reinfection, or of failure of the solution to kill spores. However, cure is so easily accomplished that many may prefer to await definite signs of recurrence, and then to repeat the treatment.

In mild cases healing is complete within a week; in severe cases within about three weeks. The surrounding skin never shows signs of damage, although it is always covered with some of the solution. Nor does the solution affect the finger that repeatedly applies it. Evidently the phenol does not penetrate deeply while still in high concentration.

The bottled solution retains its potency for at least two years. I have found that the effectiveness of the solution is almost, if not entirely, abolished when the amount of phenol is reduced by one half.

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BOOK REVIEWS

Practical Survey of Chemistry and Metabolism of the Skin. By Morris Markowitz, M.D. 8°, cloth, 196 pp. Philadelphia: The Blakiston Company, 1942. \$3.50.

The study of the chemistry and the metabolism of the skin is a comparatively new field. Since Markowitz's book is the first in the English language dealing with the subject, it will be welcomed by everyone interested in this field.

A great deal of useful information is contained in this book despite its small size. Brevity is, in some instances, an advantage of the book because, by being brief, the author restricts himself to the presentation of essential facts. Some subjects, however, are treated too sketchily. The discussion of the blood chemistry of the xanthoma group, for instance, is inadequate. Some important chemical studies, like those by Nathan and Stern and by Dörfel concerning the electrolyte content of the skin in various dermatoses, are not even mentioned. Occasionally, the author in striving for brevity is too dogmatic, as, for example, in the statements that in the blood serum of patients with urticaria the nonprotein nitrogen is increased above normal and the chlorides are decreased and that in alopecia areata the serum cholesterol is decreased. In several instances the author breaks his stated resolution to omit hypotheses. He even discusses subjects entirely unrelated to dermatology, such as the clotting of the blood of Crustacea, the difference between Gentile and Jewish blood, and congenital (fecal) steatorrhea, to which he devotes a "chapter."

The extensive bibliography is a valuable part of the book. Its value would have been still greater if the titles of the quoted papers were given in all instances. The foreign references, unfortunately, contain literally hundreds of typographical errors.

American Jewish Physicians of Note: Biographical Sketches. By Solomon R. Kagan, M.D. 8°, cloth, 304 pp., with 129 portraits. Boston: Boston Medical Publishing Company, 1942. \$5.00.

This book, a series of three hundred and sixteen brief biographical sketches, some of which are illustrated with portraits, is a supplement to the two editions of the author's previous volume, *Jewish Contributions to Medicine in America*, published in 1934 and 1939. A "Medical Chronology," from 1887 to 1942, is incorporated as an appendix. The subjects are well chosen, including such distinguished names as Isaac Hays, Abraham Jacobi, Simon Baruch, Samuel James Meltzer, Frederick Forchheimer, Howard Lilienthal, Max Einhorn, Simon Flexner, Milton Joseph Rosenau, Leo Loeb, Joseph Bolivar De Lee, Bela Schick and Morris Fishbein. The work is an impressive tribute to the contribution of the intellectual Jewish race to the progress of medical science in America. Perhaps the work might be made more useful and valuable by arranging the biographies alphabetically.

The Hand: Its disabilities and diseases. By Condict W. Cutler, Jr., M.D. 8°, cloth, 572 pp., with 274 illustrations. Philadelphia and London: W. B. Saunders Company, 1942. \$7.50.

In this book the author has made the ambitious attempt to discuss every injury and disease that may result in disability of the hand. With his wide experience in the

treatment of functional disturbances of the hand, the author has come closer to his aim than have the authors of most treatises. A more closely knit and a more useful reference book would have resulted if he had devoted his attention only to those things that are commonly seen and are known to result in serious disability. The chapters on acute infections and acute injuries are excellent; however, there is marked disproportion in the emphasis given to other conditions. Unknown and rarely seen diseases are described at length, whereas infantile paralysis and chronic arthritis are dismissed with a few paragraphs. Although great manual disability often results from these latter diseases, apparently the author is ignorant of this and of the voluminous literature that has been written on the rehabilitation of the hand following these diseases.

The illustrations are clear and for the most part well chosen. All but a few of them, however, have been borrowed from the writings of other men. A much stronger and more interesting book would have resulted if the author had drawn more on his experience and had supplemented this with illustrations of his own. Each chapter has a fairly complete bibliography of pertinent literature.

This treatise should prove to be a useful reference book to surgeons who are called on to treat disabilities of the hand.

Gynecology with a Section on Female Urology. By Lawrence R. Wharton, MD. 8°, cloth, 1006 pp., with 444 illustrations. Philadelphia and London: W. B. Saunders Company, 1943. \$10.00.

This book is divided into sixty-five chapters, a number of them being preceded by a synopsis, and each being followed by an essential bibliography.

The chapter on anatomy is well done, its illustrations have been borrowed largely from other works, but were wisely chosen. The chapter on embryology is concise and clear, the subject of female hormonology is brought up to date and as here presented is readily within the grasp of the medical student. Twenty-seven pages are devoted to menstruation, functional uterine bleeding and hyperplasia of the endometrium are fully discussed, and dysmenorrhea is extensively covered from the standpoint of etiology and of treatment, conservative treatment being emphasized. The treatment of the menopause, both natural and artificial, receives due consideration. A chapter is given over to the sympathetic nervous system in gynecology and female urology, and the operation of presacral neurectomy is clearly illustrated. The injuries of childbirth are graphically explained, their nonoperative and operative treatment are described, and methods of operation are suggested, those advocated by George Gray Ward receive considerable prominence. The importance of free dissection and the use of fiscal structures are emphasized both in the text and the illustrations.

The author assigns 37 pages to uterine prolapse. Here special emphasis is placed on four methods, namely, the interposition operation, the Ward modification of the Mayo vaginal hysterectomy, Richardson's composite operation, the parametrial fixation, or the Manchester operation. Misplacements of the uterus are treated conservatively in uncomplicated cases, whereas suspension operations of which a number are described are reserved for complicated ones.

The newer methods of treatment in pelvic infections—gonorrheal, tuberculous and puerperal—are extensively discussed and illustrated. Diseases of the vulva, the vagina and the uterine cervix are well brought out, with a chapter on pruritus. Genital fistulas, both urinary and fecal, are mentioned, and a plan for their repair is satisfactorily outlined.

The section on carcinoma of the cervix, which comprises its classification, histology, diagnosis and treatment, is especially well done, and treatment of carcinoma of the cervix in pregnancy is in accord with recent views. Sixty-four pages concern diseases of the uterus, myomas being freely discussed and illustrated, and uterine sarcoma receiving due consideration. In the management of carcinoma of the endometrium, panhysterectomy with removal of the adnexa and a cuff of vagina is recommended, whereas irradiation is reserved for poor surgical risks. Irradiation before surgery is advised whenever feasible, since many patients are thereby so improved that operation becomes possible. It is used postoperatively as indicated.

There is a chapter on hysterectomy, abdominal and vaginal, in which the technic of abdominal hysterectomy is profusely illustrated. Individualization of cases is recommended, and a conservative approach is advised in the choice between supracervical hysterectomy and panhysterectomy for benign uterine lesions. Diseases of the fallopian tubes are adequately described in a separate chapter.

A great deal of space is given to tumors of the ovary. The historical section makes interesting reading; the common rare tumors are described and the classification given is simple and easily comprehensible.

All the known tests and methods of treatment in connection with sterility are thoroughly explained and included in an 18-page chapter on abortion, not commonly found in the average textbook on gynecology. There can be no valid objection to its inclusion since the gynecologist is constantly called on to treat abortion. In this book it is covered as completely as it is in most books on obstetrics.

A favorable impression is gained from the interesting chapter on postoperative care, and the gynecological part of the book is concluded by a discussion of the normal hygiene of healthy women.

The second section covers anatomy and methods of urologic diagnosis, and the relation of the urinary organs to the pelvic organs is stressed. In the description of cystoscopy the Kelly air cystoscope is used. It is true that this method developed at the Johns Hopkins University School of Medicine is still extensively employed there for examination of the bladder and catheterization of the ureters, but most investigators trained elsewhere prefer the water cystoscope, realizing that the lithotomy position employed with the water cystoscope is more comfortable for the patient than is the knee-chest position in which she is placed when the air cystoscope is used. This section on urology is complete and well illustrated, and may serve as ready reference.

There is but little in this book with which the teacher of gynecology would not agree. It is well prepared and illustrated and should be easily understood by the medical student. For the general practitioner it affords a ready reference to the important problems of gynecology, including female urology, and it deserves a place in the library of the specialist.

Blood Substitutes and Blood Transfusion. Edited by Stuart Mudd, M.D., and William Thalhimer, M.D. 8°, cloth, 407 pp., with 97 illustrations, 6 charts, 60 tables and 6 graphs. Springfield, Illinois: Charles C Thomas, 1942. \$5.00.

This book is a compendium of work presented at a symposium in 1941. The preliminary discussions of the pathologic physiology of shock consist of reports of experimental observations by several authorities. These are well-known studies but in fragmentary form and not meant to be comprehensive; rather they are introductory to the many other chapters of the book concerned with methods of blood-volume restoration. These chapters therefore are not of too great importance in themselves because they are so incomplete and by no means up to date.

The various succeeding chapters contain a large amount of detailed technical information on the preservation, storage, freezing and drying of plasma, which should be useful to hospitals, defense centers and so forth. However, they are not especially useful for the individual clinician.

There are many good discussions of the chemistry and separation of plasma proteins. A report of preliminary work on hemoglobin as a plasma protein substitute is presented. The preliminary clinical testing of beef albumin encouraging enough to warrant further trial is recorded, but the results of more recent trials are not available. Early reports of the utilization of casein digests to form plasma protein are to be found in the discussion, but these have been greatly supplemented in the current surgical literature. The necessity for good large-scale methods of providing adequate supplies of properly processed plasma or effective plasma substitutes is stated from the civilian and military points of view. There is an excellent discussion of bacteriologic problems involved in the collection and storage of whole plasma. Likewise, the problems of storage of whole blood are described, including the biochemical, morphologic and immunologic changes that occur in stored blood. The discussion of special aspects of blood type in whole-blood transfusion is extremely valuable, and includes a consideration of universal donors, of neutralizing type-specific antibodies, of improved methods for typing serum and of the Rh factor.

The clinical reports on the use of stored plasma lend credence to the general knowledge that the various kinds of stored plasma are safe to give. Practical problems are discussed in case reports. Because of the detailed technical information, the book should be useful for persons or institutions interested in establishing a blood bank or plasma supply. And it should be helpful to physicians or surgeons because it presents a good outline of the problems of blood substitutes and because it gives a good discussion of methods to establish the compatibility of whole blood. It contributes little to a consideration of the shock problem or of the usefulness of blood substitutes in shock since most of the reports are too preliminary and there are no extensive clinical or experimental data.

In general, this book has the faults and advantages of a compendium. It is uneven—many sections bear little weight because of the preliminary nature of the reports, and many sections are of interest to a few only because of their technical character. On the other hand, it has the advantages of containing a good deal of in-

teresting and useful information that is easily reached by reading the appropriate section.

Diseases of the Skin. By Frank Knowles, M.D., Edward F. Corson, M.D., and Henry B. Decker, M.D. Fourth edition. 8°, cloth, 621 pp., with 272 illustrations. Philadelphia: Lea and Febiger, 1942. \$7.00.

In the fourth edition of this textbook, Drs. Edward F. Corson and Henry B. Decker have been added as co-authors.

The book begins with an introductory chapter dealing with the anatomy, physiology, diagnosis and therapy of skin diseases. Fourteen chapters describing the various classes of cutaneous disease, with a discussion on new conditions, under twenty-seven additional headings, have been added in this edition. A short reference to vitamins in relation to skin diseases and the use of sulfonamide drugs in therapeutic measures are included in the introductory chapters.

Tropical skin diseases are discussed, and the chapter on the treatment of syphilis is especially valuable to the general practitioner since practical plans for the therapy of all stages of the disease are presented in detail.

The book, although relatively small for a textbook, furnishes a description of all the skin diseases in a more concise form than is found in the larger textbooks on dermatology.

The bibliography consists of a limited number of references, and twenty-one new engravings have been added. The photographs are unusually clear, but there is a lack of histologic plates, which many readers are especially interested in today since dermatopathology is stressed as an important field in the study of skin lesions.

This volume is recommended as a textbook for the medical student and will be particularly useful to the practitioner of medicine because it gives the necessary information in a readable, concise form.

Mark Pfeiffer, M.D. By John Weld. 8°, cloth, 324 pp. New York City: Charles Scribner's Sons, 1943. \$2.75.

This is a novel of a young doctor from the Middle West who gets his final training in Chicago and marries a wealthy, snobbish, unprincipled woman in place of a fine nurse, his first choice. Finally the marriage breaks up, as it was bound to do, and he returns to his first love. This is a rather straightforward, simply written novel with a medical background. The characters are not particularly well drawn and the story is one that will not excite interest. There is too much emotionalism, drinking, marital infidelity and bad language.

Of slight interest to doctors, however, is the depiction of Howard Kendrick, a neurosurgeon from Boston. This is quite obviously a portrait of the late Harvey Cushing. The hero of the book comes to work with Kendrick for a year, and in the following chapters there are remarks and some action characteristic of one aspect of Cushing's life; however, the author has missed much of the real man behind Cushing's mannerisms. The hero of the story is impressed by Kendrick's character and his future life is guided by what he unconsciously absorbed under Kendrick's tutelage. As this book is dedicated to Dr. Loyal Davis, it is presumed that he may have been helpful to the author, as a former student of Dr. Cushing.

(Notices on page viii)

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PULMONARY EMBOLISM DUE TO QUIET VENOUS THROMBOSES AND SIMULATING CARDIAC AND PULMONARY DISEASE

JOHN HOMANS, M.D.*

BOSTON

PULMONARY embolism is often caused by quiet thrombosis in the legs. As a complication of operation, injury or illness, this accident is well recognized. But embolism due to quiet or silent thrombosis may also occur in seemingly well persons. Before any signs of thrombosis appear, it may recur again and again or may prove fatal at a single episode. Embolism from such a thrombosis is more apt to cause repeated pulmonary infarction without fatality than that which complicates operation, accident or illness. Yet it may end fatally. Its symptoms sometimes imitate coronary occlusion and sometimes pulmonary disease. It may even take on one appearance or the other in successive episodes in any one patient.

For some years, Dr. Paul D. White has been calling attention to the frequency of pulmonary embolism and infarction. In a recent paper, which reviews twenty years of his personal experience, he¹ indicates that the medical profession has been backward in paying attention to these serious accidents. He notes his own rapidly increasing number of observations in cases that he would formerly have diagnosed as congestive heart failure or pneumonia. In respect to the simulation of heart disease by embolism, White finds that in 75 definite cases of embolism, most of which he has observed during a recent ten-year period, 28 simulated and 47 complicated heart disease. He finds clues to the diagnosis of embolism in periodic attacks of faintness or dyspnea or prostration, or in attacks of unexplained fever and leukocytosis or even jaundice (from hemolysis of the infarct and an engorged liver). It will be noted that these are not conventional symptoms of pulmonary embolism.

The very fact that White, as a cardiologist, sees cases in consultation that other physicians have diagnosed as angina, coronary occlusion or pneu-

monia has given him the opportunity to distinguish many cases of embolism masquerading as heart disease, and he has put up to surgery the task of discovering and removing the source of embolism in such circumstances. He has squarely stated the problem when he says, "Peripheral phlebitis was evident in only a few cases, but it is probable that the majority might have shown such a lesion if we could have explored the veins; at least, that is the lesson to be derived from the post-mortem findings at the Massachusetts General Hospital, where 70 per cent of the medical pulmonary embolism cases have phlebitis that gives no evidence of its presence."

In support of this aspect of the subject, Hampton and Castleman,^{2,3} from their exhaustive combined roentgenologic and pathological study of pulmonary embolism and infarction, are finding these lesions in increasing numbers. They hold that there need be neither a combination of pleural pain and blood spitting nor any obvious source of embolism, but that given any clue, and with roentgenologic evidence, a diagnosis may be made. One of their conclusions is pertinent here. They say, "In view of the fact that one-third of the cases of pulmonary infarction occur in patients who have not been operated upon and who have no demonstrable cardiac disease, it is important to consider pulmonary infarction in the differential diagnosis of pulmonary disease in *ambulatory patients* [italics mine]."

This paper is a sequel to one by me⁴ published in this journal in 1934 under the title "Thrombosis of the Deep Veins of the Lower Leg, Causing Pulmonary Embolism." In 3 of the 4 cases discussed in that paper, there was an element of trauma; 2 patients, not suspected of harboring a thrombosis, died of pulmonary embolism, and 1 was treated by division of the femoral vein in order to prevent a possible embolism. The fourth patient, who recovered without operation,

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reappeared with a second idiopathic quiet thrombosis in 1939, sixteen years after his first, but in the opposite leg. Eleven cases form the basis of discussion, in all of which trauma, operation and serious illness were absent or insignificant factors. "Idiopathic" is a poor term, but it connotes "of unknown origin" or "without satisfactory explanation." Barker⁵ used it in 1936 in a paper describing thrombophlebitis in ambulatory patients, but it was an old term then. Actually, the fact that an injury, operation or illness precedes thrombosis explains nothing, since no one knows why ninety-nine such episodes cause no thrombosis and the one hundredth a dangerous process. But to throw oneself into the frame of mind which admits that thrombosis in the deep veins of the legs may occur in anyone at any time, one must cease to believe that *any* recognizable etiologic factor need exist.

Quiet thrombosis, or so-called "phlebothrombosis," is a noninflammatory, reactionless process. It takes place in the deep veins of the legs, usually below the knees. In its dangerous stage, it causes little venous obstruction. Though it may occur at any age from adolescence to senescence and in persons of various physical types, it is most commonly seen in the sixth and seventh decades and in fat or fattish patients. Thus it has much the same incidence as the outspoken inflammatory thrombophlebitis, or phlegmasia alba dolens, to which actually it is related.

The peculiar and dangerous quality of a quiet venous thrombosis lies in its decided tendency to form a loose, soft, detachable thrombus. It does not necessarily form such a propagating thrombus. Indeed, it is true that thromboses often heal without accident and, occasionally perhaps, without being noticed. Many develop into an obstructive, outspoken thrombophlebitis.* The explanation of the lack of statistics warning the profession of the incidence of quiet thrombosis and consequent embolism lies in this, that the more silent the process, the greater the danger of embolism. This is almost a law. A fatal pulmonary accident may come from a leg that even those most familiar with venous thrombosis must consider normal, and by contrast, the great swollen leg of thrombophlebitis almost never causes embolism. Statistics based on *recognizable* thromboses are thus nearly useless. In the quiet process, some part of the thrombus is not adherent or is only very lightly

adherent to the vein, being partly or wholly free to float away; whereas the inflammatory thrombus is fixed by a local reaction in the wall of the vein. One should think of a quiet thrombosis as consisting of a local process occupying perhaps only a few inches of a vein, one of many among the great muscles of the calf, but possibly having a loose, soft tail that floats in the popliteal and femoral veins. On this basis, why expect to discern outspoken or indeed any physical signs in the leg? Barker et al.,¹⁰ of the Mayo Clinic, have published figures that indicate that one person in twenty in whom thrombosis is recognized will suffer from a pulmonary embolism of some degree, but these figures suffer from the defect that I have just indicated.

I propose, therefore, to deal here with pulmonary embolism as a single or repeated episode, usually from so silent an idiopathic thrombosis that the pulmonary infarct is apt to be mistaken for or confused with a coronary occlusion, angina or pleurisy. But because embolism is not the necessary or even the usual result of a quiet, deep lower-leg thrombosis, and because treatment of thrombosis, whether or not it has already caused embolism, is required, it is necessary to consider briefly the three courses that the original thrombosis may pursue, which are as follows: recovery without extension; development into phlegmasia alba dolens; and formation of a propagating thrombus with pulmonary embolism.

Recovery without extension or embolism. This may take place without operation, though among 5 cases (six episodes) so treated by me, elevation and rest failed three times (signs of thrombosis reappeared on resumption of an active life) and division of the femoral vein was then required. Two patients recovered without operation; in one of these, however, the disease appeared in the other leg sixteen years later, when conservative treatment was followed by recurrence, and at operation a soft thrombus was sucked out of the femoral vein. Considering the frequency with which embolism is associated with any one quiet thrombosis, not to speak of recurring thrombosis, this short series gives evidence in favor of immediate operation without a trial of conservative measures.† Such treatment was used only twice. However, no deaths occurred among the few patients conservatively treated, which was perhaps good luck.

Development into femoroiliac thrombophlebitis (phlegmasia alba dolens). Evidently this development is not often observed. Only twice have I

*It is now fairly well established, through the work of Rössle,⁶ Bauer,⁷ & Frykholm⁸ and others, that the great majority of venous thromboses in the legs, of all types, begin in the calf and foot; in fact, that only 10 per cent of all thromboses in the femoral vein are unassociated with deep thrombosis below the knee. Thus the quiet peripheral disease must frequently develop into the obstructive, inflammatory type. Bauer has traced this development in venographic studies. The idea is contrary to the long accepted belief that a femoroiliac thrombophlebitis usually occurs independently of any peripheral process.

†Since postoperative and post traumatic thromboses are not under discussion here, it is unnecessary to quote Fine and Sears¹¹ or Welch, Faxon and McGahey¹² in support of routine division of the femoral vein. Probably, however, most of the lessons learned from cases of postoperative thrombosis apply here, that is, to cases of idiopathic thrombosis that have not yet given rise to embolism.

noticed it clearly. Yet the Swedish investigators, especially Bauer,^{7,8} are sure that it is common, and Conner,¹⁸ in discussing his experiences with typhoidal thrombophlebitis, speaks of the frequent observation of early signs in the foot and calf before the full-blown swelling of phlegmasia alba dolens occurs. One certainly sees cases in which embolism precedes this outspoken state, that is, during an early, quiet stage.

Formation of a propagating thrombus with pulmonary embolism. This outcome is covered by the 11 cases to be presented in some detail, and with these will be discussed, incidentally, 6 cases of embolism arising from thrombosis due to injury, illness or an old thrombophlebitis. Actually, these latter behave in every way like the idiopathic sort except, perhaps, that, following an old femoroiliac thrombophlebitis, the recurrent episodes of embolism may be spread out over particularly long periods, even over many years. Postoperative thrombosis, and embolism are not considered here at all.

* * *

The following 11 brief case reports will give some idea of the nature of the problems presented and the results obtained.

CASE 1. R. M. A., a 61-year-old man, had previously been well. There was repeated embolism over a period of 3 months, at first suggestive of coronary occlusion, but with a negative electrocardiogram, and later of right-sided and left-sided infarctions. Examination of the legs was negative until 1 week before operation. There was a positive dorsiflexion sign and faint cyanosis of the left foot on standing. A bilateral process was suspected that extended above the groin on the left, as indicated by long striding disease and a cyanotic left foot.

Operation consisted of section of the left common iliac and right superficial femoral veins. A serious embolism occurred before the left iliac vein was approached. There was no thrombus at the level of division. A hurried section of the right superficial femoral vein may have caused failure to observe a thrombus in the common femoral vein. A small embolism developed on the 4th postoperative day. There was recovery with no further embolism and with excellent function. There was a slight swelling of the right leg on the side of the femoral division.

CASE 2. W. L. S., a 56-year-old man, had possible old biliary disease. There had been repeated attacks of sub-sternal pain over a period of 6 months. Coronary occlusion was suspected but not proved. There was a fall in blood pressure. Patchy consolidation of both lungs was observed. Four weeks before operation tenderness developed over the right femoral vein at the groin, without edema. Later there was a positive dorsiflexion sign, but no cyanosis. A right-sided process as high as the inguinal ligament was suspected.

Operation consisted of section of the right common iliac vein. There were no further attacks. Function of the right leg was excellent. There was subsequent development of acute cholecystitis and stone in the common duct.

CASE 3. C. W. Y., a 53-year-old woman, had previously been well. Repeated attacks of breathlessness and faintness had occurred over a period of 3 months, without pain. Examination of the thorax (by x-ray) and legs was negative until 4 days before the first operation, when the left foot became faintly cyanotic on standing. During the following days, further serious attacks of breathlessness and faintness occurred. The dorsiflexion sign in the left leg became positive. There was no edema. By x-ray, there was considerable pulmonary infarction of the right lung. The diagnosis was repeated pulmonary embolism from a quiet process in the left leg.

The first operation was section of the left superficial femoral vein. No thrombus was found at this level. Increasing dyspnea and signs of thrombosis in the right leg during the next few days led to division of the right superficial femoral vein, and again no thrombus was found. During the next 2 weeks, rising venous pressure and a wide shadow of the superior vena cava shown by x-ray examination warned that the pulmonary artery was obstructed. Cor pulmonale developed. The patient was heparinized for several days before her death.

Post-mortem examination showed the pulmonary artery and its branches to be loaded with emboli of varying sizes and ages. From the profunda femoris of each leg a healed thrombus projected into the common femoral vein. The last emboli might well have come from this source.

CASE 4. W. W., a vigorous 34-year-old man, had a bad family background of thrombosis and embolism. During the past year, three episodes of pleuritic pain and bloody sputum had occurred. X-ray examination revealed several pulmonary infarcts. The right leg, otherwise negative, gave a positive dorsiflexion sign. A venogram excited a rapid spread of the thrombosis.

Operation consisted of division of the right superficial femoral vein. No thrombus was found at this level. The patient was heparinized. Following withdrawal of the heparin, thrombosis in the calf again became aggravated. There was recovery with excellent function of the leg. No further embolism occurred, but 16 months later there were signs of thrombosis in the opposite leg.

CASE 5. C. A. G., a 55-year-old man, had a doubtful history of a superficial thrombosis 15 years previously. The first episode, 2 months previously, consisted of a fugitive lameness in the left calf, followed by an unexplained cough. Later, there were several attacks of cough and dyspnea and finally hemoptysis. A positive dorsiflexion sign was noted in the right leg. There was no swelling or cyanosis.

Operation consisted of division of the right superficial femoral vein, but no thrombus was found at this level. There was recovery with excellent function and no further embolism.

CASE 6. H. M. B., a 49-year-old man, had had two episodes of violent sub-sternal pain on successive days 3 weeks previously, with dyspnea and cough. There was thrombosis in a varicose vein of the right leg, associated with cyanosis and slight swelling of the whole right leg, and indicating thrombosis as high as the inguinal ligament.

Operation consisted of division of the right common iliac vein, no thrombosis being found at this level. There was recovery with excellent function and no further embolism.

CASE 7. T.A.W., a 55-year-old man, was suffering from a moderate arteriosclerotic deficiency. Three years previously he had experienced a supposed coronary occlusion, from which he had made a good recovery. One week before operation there was sharp pleural pain on the left side. X-ray examination revealed a pulmonary infarct. There was a positive dorsiflexion sign in the right leg, but no cyanosis or edema.

Operation consisted of division of the right superficial femoral vein and periarterial sympathectomy. No thrombus was found at this level. There was recovery with excellent function and no further embolism.

CASE 8. R.E.F., a 47-year-old man, had suffered pleural pain and hemoptysis 10 years previously, following pain in the left calf with local swelling. He was thought to have tuberculosis. Five years previously a superficial wandering phlebitis was cured by high section of the saphenous vein. Over the last few years there had been recurring pain and lameness in the left calf. The patient had had a recent attack of pain, soreness and slight cyanosis of toes, lasting for 10 days. There was a positive dorsiflexion sign. No tenderness was found over the femoral vessels.

Operation consisted of section of the superficial femoral vein. No thrombus was found at this level, but a feeble flow of blood suggested thrombosis just below it. There was good recovery with excellent function.

CASE 9. F.B., a 57-year-old man, had previously been well. Two months previously hemoptysis occurred without warning. One month later the left ankle was found to be swollen, the leg lame, and the calf tender. Conservative treatment was followed by recurrence of local signs.

Operation consisted of section of the superficial femoral vein. There was good recovery with some cyanosis of the lower leg. No further embolism occurred.

CASE 10 (previously reported³). H.L., a 55-year-old man, gave an early history of mild rheumatic fever. On the day that he noticed swelling and discomfort of the right lower leg, he was in a minor automobile collision. From that moment until his death 6 days later, he was short of breath and decidedly cyanotic. The right leg below the knee was moderately swollen, but local swelling as well as general cyanosis improved up to the moment of his death.

Post-mortem examination revealed a 30-cm. embolus that had been floating in the pulmonary artery until beginning organization and fixation had finally obstructed the vessel. Embolism must have occurred at the moment of the automobile collision. The source of embolism was a diffuse, deep thrombosis in the deep veins of the calf. There was a similar process in the veins among the thigh muscles.

CASE 11. E.D., a 63-year-old woman, had had a superficial thrombosis in the veins of the thigh for 3 weeks. There were sudden breathlessness, faintness and collapse at the end of this time. Three days later, the legs were negative for all signs of thrombosis, except for a tender mass in the left groin, which was proved at operation to be a canalized fresh thrombus at the root of the great saphenous vein. A propagating thrombus had probably broken off in the femoral vein.

Operation consisted of section of the great saphenous vein. There was recovery with no further embolism.

Among the 11 idiopathic cases, there were 9 men, and in the whole group of 17, only 3 women, yet when women were affected, the result was always serious.

The ages of the combined groups ran from twenty-eight to sixty-three. Only 3 of the idiopathic group were under fifty and the 2 patients who died of embolism were, respectively, fifty-three and fifty-five. In the secondary group, the 1 patient who died of embolism was fifty-three. In this same group, a man of twenty-eight developed a thrombosis as a result of whooping cough and suffered a pulmonary infarction, but he had attempted to cure his disease by playing squash rackets.

Multiple embolism occurred six times in the idiopathic group. There seems to be no rule as to the seriousness of the individual episodes. In 1 case, after many small embolisms, spread out over three months, had left no trace in the lungs by x-ray examination, an accumulation of many fragments, coming from both lower legs and perhaps from the veins of both thighs, finally, in spite of division of the femoral vein, plugged the pulmonary arteries, with a fatal result. With one notable exception (Case 1), in the other 5 cases of multiple embolism there was little damage, and all patients recovered after vein division. One single embolism was fatal. Small and rather harmless single embolism occurred 3 times.

In the supplementary group, multiple embolism occurred four times. In 3 such cases, all of thrombosis following an old femoroiliac thrombophlebitis, vein division was followed by recovery. The fourth, an obscure case in which infarction followed an acute enteritis, was subjected to heparinization without operation, and the patient died of pulmonary embolism. In the fifth and sixth cases, infarction was small and unimportant.

As between cardiac and strictly pulmonary symptoms, it would seem that when an embolus causes a true anatomic, pulmonary infarct, a pleuritic type of pain usually results. Then there is little suggestion of angina or a coronary occlusion. But emboli do not necessarily obstruct either large or small pulmonary vessels, at least in the sense that they create a bloodless, airless pulmonary area visible on roentgenography, and so they are apt to cause substernal agonizing pain, or fainting, or breathlessness, or some combination of these symptoms. Cough and expectoration of blood may occur after any initial symptom or without any earlier symptom.

The electrocardiogram is helpful to the cardiologist. In pulmonary embolism, appearances characteristic of coronary conclusion are absent. A

normal electrocardiogram is, of course, consistent with pulmonary embolism, but serious obstruction to the pulmonary circulation by emboli, causing embarrassment to the right side of the heart—that is, *cor pulmonale*—gives characteristic signs. It is necessary in that case to be sure that the emboli have not arisen in the right heart itself.

X-ray study is remarkably helpful in making a positive diagnosis of pulmonary infarction. Yet a clear lung field is consistent with serious and repeated embolism.

Failure of even massive emboli to cause death for many days, or even for weeks and months, has appeared twice in the idiopathic series. In one case,* that of a man of fifty-three, slight cyanosis and breathlessness were initial symptoms. During the following six days, recovery seemed to be taking place, but at the end of this time a typical embolic death occurred. Autopsy showed a partly organized embolus, a foot long, floating in the pulmonary artery, which it had finally obstructed. In another case a woman of fifty-three, after repeated embolism for three months and an unsuccessful bilateral division of the femoral vein, finally died. For most of the last weeks of her life, she had been breathless. *Cor pulmonale* was evident, but the lung fields, as previously told, for a long time, were clear. Autopsy showed quantities of organized thrombi fixed in the pulmonary arteries. Here again, full obstruction was greatly delayed.

The effectiveness of vein division. Among the 11 idiopathic cases, division of the femoral, external iliac or common iliac vein was practiced in 10 patients. In the eleventh, as is related in the protocols, the patient's cyanosis gave rise to a suspicion of some cardiac disorder, and operation was not attempted. This was fortunate; for the great embolus was already in the pulmonary artery.

In 1 of the 10 cases subjected to operation, as already told, many emboli had already entered the pulmonary artery before operation was undertaken. Then the superficial femoral veins of both legs were successively divided and, there being no thrombus in the femoral, distal to the profunda, there seemed no need of interrupting the vein at a higher level. However, as the subsequent autopsy showed, a thrombus, starting in the profunda, had already entered each common femoral vein or subsequently did so. Therefore, when embolism is of long standing and perhaps when thrombosis is thought to have been going on for weeks or months, the vein certainly ought to be divided proximal to the profunda or even higher. The point will presently be discussed. In any event, among the 11 cases, this was the only one, curable

perhaps by surgery, in which death occurred and further embolism was not prevented.

In the secondary group, all the patients subjected to surgery recovered. One patient, treated by heparin alone, died.

The level of vein division. In the usual case, when one or more episodes of embolism have occurred and local signs point to thrombosis in one leg, it is sufficient to divide the superficial femoral vein. As this is done, an examination should be made to detect thrombosis at the level of division. If no thrombus is present below the profunda or at the level of the profunda, division of the superficial femoral is satisfactory. One is also led to be satisfied with this procedure because it disturbs the venous return very little; whereas, if the common femoral vein is divided, proximal to the profunda, serious congestion and swelling often follow, especially if no old thrombophlebitis has preceded, building up a collateral venous pathway.

There are two possible sources of accident in case of division of the superficial femoral vein in the leg showing clinical signs of thrombosis: a separate deep thrombosis in the thigh, already present or to occur later, may give rise to future embolism; there may be a separate, silent thrombosis in the opposite leg.

In respect to the first of these accidents, Frykholm⁹ has shown that an independent thrombosis not at all rarely starts in the deep muscular veins of the thigh, whence it enters the common femoral by way of the great profunda branches. How often this complicates a deep thrombosis originating in the lower leg is not known, for when one finds a thrombosed, partly obstructed profunda in exploring thrombosis of the superficial and deep femoral veins, there is no saying whether thrombosis has started independently in the profunda or whether a retrograde thrombosis has backed up into it. I am inclined to think, therefore, that in old thrombotic processes attended by embolism, one should always divide the common femoral vein above the profunda or go even higher. This latter procedure I shall presently discuss.

In respect to the second possibility—namely, that the second leg is involved—this is anyone's guess. I have not as a routine explored the femoral vein of the second leg when that leg shows no sign of disease and when the evidence for thrombosis in the leg already subjected to operation is good. Nevertheless, a silent process in the second leg may actually be the source of embolism at the time the first is subjected to operation. For example, if embolism is still taking place when the first leg is already considerably swollen as a result of a process now becoming obstructive in the veins

*This case was reported in the previous paper.

of the groin and pelvis, this really exonerates the swollen leg; for embolism seldom occurs from an obstructive thrombosis or thrombophlebitis. Therefore, the place to look for the *present* source of embolism is the second, or innocent-appearing, leg. This perhaps is the time to use venography. But I should be perfectly willing to explore and divide the superficial femoral vein of the second leg without venography under the conditions just outlined.

Division of the common or external iliac vein. This procedure has been carried out eight times in the combined series. The right common iliac vein has been divided six times, the left common iliac and the left external iliac each once. I propose, in a subsequent publication, to make a special study of these operations. It is enough to say of them here that: division of the common iliac is the operation of choice in processes of considerable age when thrombosis is believed to have occupied, without altogether obstructing, the common femoral vein; division of the common iliac in particular offers a better collateral venous return than division of the common femoral; division of an iliac vein is not much harder to perform than is division of the common femoral, since it can be carried out extraperitoneally; and the higher division gives the patient and surgeon an assurance of safety, lacking in even a common femoral division, since, almost invariably, the thrombosis has not mounted to the level of operation. The above is especially applicable to right-sided processes, for not only do these tend to mount less high than left-sided ones, but the right common iliac vein lies lateral to the artery and is easily accessible by an extraperitoneal approach. As for the left-sided thromboses, I have been in considerable doubt as to the advantage offered by interruption of the common iliac vein. However, experience has assured me that when a comparatively old process is already present at the groin, the operation is decidedly worth while. In the first place, one can usually divide or ligate the left common iliac vein proximal to the thrombus; and in the second, although the vein lies median to the artery and rather over the edge of the pelvis, it is still reasonably accessible by the extraperitoneal operative approach. The chief difficulty that I have encountered lies in dealing with a friable vein that has been the seat of an old inflammatory

thrombophlebitis. Adherent and easily torn, its deep situation makes its isolation a delicate matter. Doubtless further experience will throw light on such problems.

SUMMARY

An account has been given of 11 cases of quiet thrombosis in the lower limb causing pulmonary embolism in ambulatory patients. With these cases are discussed 6 others of similar character but in which an old thrombophlebitis, an injury or an illness had preceded the thrombosis.

Consideration of all these cases shows that since pulmonary infarction and embolism often simulate cardiac and pulmonary disease, in ambulatory patients otherwise well, they must be considered in the differential diagnosis of many acute and recurrent thoracic disorders.

It may reasonably be concluded from this short series of cases that: repeated embolism, associated with quiet thrombosis, is not rare; the dangerous or fatal quality of any one process is unpredictable; operative treatment, to secure interruption of the thrombosed vein proximal to the source of embolism, is always indicated; conservative treatment, even if not followed by further embolism, is unlikely to prevent continuance or recurrence of the thrombosis; and the use of heparin does not protect against repeated embolism and a fatal outcome.

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THE HEALTH EXAMINATION OF ADOLESCENTS*

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DURING recent years there has been an ever-increasing interest in health examinations,¹ but most of the emphasis has been put on the care of infants, children at the grade-school level, college students, and adults who have reached the age when the disorders of senescence may be expected to develop. School health examinations are usually confined to a limited inspection of children in the primary grades; it is unusual, except in a few preparatory schools, to find adequate health examinations given to students at the high-school level. This relative neglect of the adolescent becomes more serious because of the unfortunate division of responsibility for his care that now exists between the pediatrician and the physician who ordinarily cares for adults: over a period of a few years during which physiologic and psychologic changes are at their height, the adolescent does not have either the advantage of a school health examination or the special attention of a physician whose primary interests and training are immediately concerned with the peculiarities of adolescence.

Another reason for the widespread neglect of health examinations in the adolescent group is the apparent health of most of these persons: their appearance seems to have led many to believe that a careful health examination will be fruitless. It seems obvious that, apart from the educational value of the annual health examination,² it is also valuable because it both permits the discovery and correction of any defects that interfere with optimal function and provides an opportunity of making the subjects cognizant of any irremediable conditions that might subsequently exclude them from certain civil or military careers.

The importance of such examinations can be readily appreciated by the study of the findings now being made by those who have examined young draftees, and this report, which concerns the findings at the health examination of 910 preparatory-school boys of the thirteenth-to-eighteenth-year age group, appears to furnish further evidence of the value of such a procedure. It should be remembered that the data are obtained from members of an economically privileged group, and that consequently the percentages for those conditions that may be affected by economic status are probably

lower than those that a survey of the general population would supply. In addition to a discussion of the findings at the health examination, a note concerning functional physical fitness is included: it seems desirable to include an estimation of the ability of each subject to perform and to recover from brief exhausting work in any thorough examination, and to avoid the error of basing one's estimate of fitness only on observations made when the subject is at rest.

METHOD OF EXAMINATION

Each year about 725 students are examined; about 250 of these have entered the institution for the first time and are given their initial examination. It has been found possible to examine about 50 of these students in a period of four hours and a half; an attempt is made to schedule twice as many boys who have been examined on previous years as new students. A student is first given his examination sheet, his name and age are recorded, and he is sent to a trained technician for an eye examination. At this examination his vision with and without glasses, his vision through a +1.50 lens and his muscle balance at both near and distant vision are determined and recorded on the examination sheet. The technic used is similar to that recently described by Sloane.³ A nurse experienced in the use of a II-A audiometer tests the hearing of each new student and of all others known to have had ear disease or impairment of hearing in the past. Recently it has been difficult to obtain dental assistance, but when possible bitewing x-ray examination and a manual examination are included as the next procedure. The student then disrobes and goes to an assistant who records his weight, height and color vision.⁴ He next goes to a physician who inspects his skin, nose and throat and examines his heart, lungs, abdomen and extremities in the conventional manner and sees that a urine specimen is collected. Following this examination the student brings his record, on which considerable data have been recorded, to another physician, who reviews all the facts, examines the reports that have come from parents and family physician, and checks any abnormal findings. In addition, he asks a few questions concerning past health, habits, interests and social relations that are designed to bring out attitudes and personality traits indicating present or future psychologic difficulties. Valuable

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suggestions regarding such an appraisal can be obtained from a recent report of the Grant Study.⁵ After this conference the student receives a lung x-ray examination and any other x-ray or blood studies that are necessary. It is possible for two physicians to examine in a relatively thorough manner a large group of students within a short time, because many of the details of the examination are handled by trained assistants. It is found necessary to have a small number of students return for a more thorough investigation of some disorders: students requiring determinations of

Such a health examination as outlined above is time consuming and relatively expensive and should not be continued unless its results justify the expenditure. In Table 1 are listed findings made at the health examination of 910 boys.

The importance of the relation of weight to health can be overemphasized, but it is certainly advisable to follow the weight trend of those students who are obviously too thin or too fat. Assignment to either of these groups is made on the basis of general appearance and not on the deviation from standards given in height-weight-age

TABLE 1. Summary of Findings at the Health Examination of 910 Boys Ranging from 13 to 19 Years of Age.

FINDING	No. of SUBJECTS	Pcr CENT	FINDING	No. of SUBJECTS	Pcr CENT
Overweight	57	6.3	Duodenal ulcer	1	0.1
Underweight	54	5.9	Fibroma of preperitoneal tissues.....	1	0.1
Visual defects:			Hydrocele	2	0.2
Color vision deficient	48	5.3	Varicosities of abdomen.....	1	0.1
Vision with glasses, one or both eyes:			Undescended testes:		
20/30	54	5.9	One	4	0.4
20/40 or less	37	4.1	Both	1	0.1
Vision with no glasses, one or both eyes:			Posture defects:		
20/30	11	1.2	Severe	10	1.1
20/40 or less	17	1.9	Moderate	60	6.6
Hypermetropia with no glasses	70	7.7	Slight	270	29.6
Heterophoria	43	4.7	Recurrent shoulder dislocation.....	3	0.3
Dental defects (based on the examination of 354 boys):			Lower-back strain	4	0.4
Caries:			Muscular atrophy (after injury).....	3	0.3
Attention urgently needed.....	64	18.1	Flail ankle and knee (poliomyelitis).....	1	0.1
Attention needed	290	82.0	Cavus foot (poliomyelitis)	1	0.1
Orthodontia needed	44	12.4	Pott's disease	1	0.1
Tonsillectomy advised	21	2.3	Impacted bullet (femur)	1	0.1
Adenoidectomy advised	3	0.3	Cervical rib	1	0.1
Marked deviation of nasal septum.....	4	0.4	Hammer toe	3	0.3
Chronic severe allergic rhinitis.....	8	0.9	Unreduced elbow dislocation	1	0.1
Nose fracture with obstruction.....	1	0.1	Osteochondritis dissecans	2	0.2
Deformity of nasal septum and ear.....	1	0.1	Osteoma:		
Dislocation of nose (anterior quadrilateral car- tilage)	1	0.1	Femur	1	0.1
Perforation of eardrum	2	0.2	Tibia	1	0.1
Auditory defects:			Cyst of femur	3	0.3
Loss of 20 d.b. or more (high tones only) ..	23	2.5	Epidermophytosis (moderate or severe).....	108	12.0
Loss of 20 d.b. or more (all tones).....	15	1.7	Eczema	4	0.4
Asthma	27	3.0	Pityriasis	2	0.2
Hay fever	91	10.0	Fibroma of posterior skull	1	0.1
History of intimate contact with tuberculosis...	21	2.3	Impetigo	1	0.1
Positive tuberculin test (0.01 mg. O. T.) (680 boys tested)	177	26.0	Acne:		
Definite history of rheumatic fever.....	15	1.6	Severe	65	7.1
Rheumatic heart disease	6	0.7	Mild	164	18.0
Congenital heart disease	2	0.2	Pigmented mole	2	0.2
Dextrocardia	2	0.2	Pilonidal sinus	20	2.2
Hypertension:			Albuminuria:		
Severe	1	0.1	Transient	45	4.9
Slight	2	0.2	Orthostatic	27	2.9
Enlarged spleen:			Diabetes	2	0.2
Acute mononucleosis	1	0.1	Endocrine disorder	5	0.5
Etiology unknown	3	0.3	Personality disorder:		
Inguinal hernia	3	0.3	Moderate	21	2.3
			Slight	40	4.4
			Speech defect (stuttering):		
			Severe	5	0.5
			Moderate	10	1.1

the basal metabolic rate are asked to spend the night before the test at the infirmary; those with albuminuria are also asked to return so that urine specimens may be obtained before arising; those with orthopedic defects or disorders of the ear, nose or throat are re-examined as groups by visiting specialists; and those failing the vision tests are referred to a competent specialist for a more thorough examination.

RESULTS

Any medical procedure that becomes routine should be subjected occasionally to critical analysis.

tables; individual students because of their constitutional type and heredity and endocrine peculiarities vary tremendously in rate and type of development, and it seems to be most satisfactory to assess these persons by observation rather than by means of a chart. Those boys whose weight is considered abnormal are given a few suggestions and their weight is rechecked at appropriate intervals. Twelve per cent of the student body showed sufficient variations in weight so that their condition justified some further attention.

Boys with a deficiency in color perception (53 per cent of the group reported here) are told of the

presence of this condition and advised that it may exclude them from certain careers. The testing of visual acuity is most important: 1.9 per cent of the group were found to have no better than 20/40 vision in one or both eyes and yet did not have glasses; many of those who did have glasses had a corrected vision of only 20/40 or less, which in many cases could and should have been more adequately corrected. Many with hypermetropia or marked heterophoria were referred for a more thorough examination, and all those who had definite symptoms of eyestrain were referred to a specialist regardless of the findings at the time of the vision test.

The importance of including a careful survey of the teeth in any health examination needs little comment; that 18 per cent of a group of 354 students needed dental care urgently, and that many others had conditions requiring attention is further evidence of the need for paying special attention to the teeth of members of this age group regardless of their economic background. A more detailed report of these findings has been published elsewhere.⁶

Tonsillectomy is advised only either when obviously diseased tonsils are present or when moderately diseased tonsils are present and there is a history of frequent infection of the upper respiratory tract or rheumatic fever. In this group about 80 per cent had previously had a tonsillectomy. A small number of nasal deformities that should have been corrected were found; because of the age group, the number of septum operations advised was small.

The percentage of boys with severe asthma or hay fever was high. Many are urged to attempt to determine the value of desensitization procedures while the facilities of a school health service are available.

The testing of hearing, like that of vision, is particularly important among students. A list of boys with impaired hearing is sent to the school administration so that proper seating in classrooms can be provided; 1.7 per cent were found to have a considerable diminution of hearing.

The percentage of students having rheumatic heart disease was small; every effort is made to have these boys maintain an objective attitude toward their condition, and restrictions are lifted rather than imposed. All those who have had rheumatic fever are urged to report at the onset of any infection of the upper respiratory tract, and an attempt is made to have all those who have rheumatic heart disease take part in athletics just as do all other members of the student body.

Definite hypertension is unusual in this age group. Those unaccustomed to medical exam-

inations are often apprehensive, and may be found to have an abnormal blood pressure, but a persistent hypertension in a relaxed adolescent is certainly rare, and should be carefully investigated before one decides that it does not rest on an emotional basis.

Lung x-ray studies of members of this group revealed little disease but because they can be compared to subsequent films taken when disease is suspected, they may be of great value. Occasionally such findings as dextrocardia, cervical rib, small areas of pneumothorax or even extensive healed miliary tuberculosis were noted. Five members of a special survey group of 680 students were found to have the combination of a negative tuberculin test, pulmonary calcification and a positive skin reaction to coccidioidin.⁷ Twenty-six per cent of this group were found to be positive to 0.01 mg. of old tuberculin.

Examination of the abdomen and genitalia reveals only a small percentage of abnormalities, but the majority of these defects are important because they can and should be corrected. It is usually desirable to correct an inguinal hernia when it is found at this age, and testes that have not descended by the time secondary sex characteristics have developed are best treated by surgery; in younger boys hormone therapy is worthy of a trial. The finding of a benign fibroma in the abdomen is unusual, but again emphasizes what may be found when a reasonably careful examination is made.

A small number of orthopedic defects may be expected. Operative treatment for recurrent shoulder dislocation is advised when the dislocation occurs frequently or when the student expects to enter such an institution as the United States Naval Academy. Osteomas are only rarely seen; surgical removal is advised if the area is exposed to frequent trauma. Many of the more severe postural defects can be considerably benefited by proper corrective procedures.⁸

The importance of observing heavily pigmented moles and sometimes advising their removal is obvious. Acne is found more frequently in the more mature boys (about 88 per cent of the acne noted occurred in students who were classified as "mature"), and presents a real problem because of its psychologic implications, particularly for those whose adjustment is not satisfactory. The percentage of students who have a pilonidal sinus and who will subsequently develop a pilonidal abscess is problematical, but at present it is well for those who contemplate a career in aviation to know that such a condition is present.

When albuminuria is found in the first urine specimen, several other specimens are collected; if albumin persists, an orthostatic test is done. Of

those with persistent albuminuria, almost all will be found to be free of albumin when an early morning specimen, collected before arising, is examined. The insignificance of these findings has been commented on by Derow,⁹ but the condition continues to be a source of difficulty when application for life insurance or for admission to some institutions is made. The finding of glycosuria is very rare, but is certainly of sufficient importance so that this test should never be omitted. In this group 1 such case, previously unrecognized, was found.

A reasonable amount of experience with members of this age group and the utilization of a short series of well-selected questions enable one to detect the majority of those students who will have difficulty in adjusting to a boarding-school situation. It might be expected that few boys with personality disorders would seek admission to a secondary school of high standards where competition is keen. That about 6 per cent of this group appeared to lack the attributes necessary for a completely satisfactory adjustment indicates how desirable it is to attempt to estimate the subject's personality in any health examination.

Abnormalities in speech are easily detected, and are always worthy of attention. Stuttering obviously interferes with a student's scholastic efficiency and his proper adjustment; personal attention and adequate therapy can be expected to improve speech as well as to bolster the stutterer's morale.

The observations made at this examination do not permit a complete answer to the question of the student's fitness and do not give all the data by which one may answer his question, What condition am I in? It is desirable also to determine his ability to perform and to recover from brief exhausting work; that is, to test the efficiency of his cardiovascular and respiratory response to exercise. A simple but relatively accurate method of testing this type of dynamic physical fitness in boys has recently been described.¹⁰ A reasonable estimate may be obtained by utilizing the formula:

$$\text{Fitness index} = \frac{\text{Duration of exercise (seconds)} \times 100}{\text{Sum of three pulse rates during the subsequent 4-minute rest period}}$$

The exercise consists of stepping up to and down from a platform thirty times a minute; the usual duration is 4 minutes (240 seconds).

Table 2 lists the distribution of scores obtained when such a test is given, and indicates the wide range of dynamic physical fitness that obtains in such a group of boys, all of whom are apparently in good health. The desirability of obtaining this type of information before any student is given

an estimate of his condition is obvious; a crew captain may appear to be equally healthy and in equally good condition in June after three months of rowing and in September after two months of farming, but his dynamic fitness will be found to be very different at each of those times. So also the convalescent following the optimum per-

TABLE 2. *Distribution of Physical Fitness Test Scores of 609 Boys Ranging in Age from 13 to 19 Years.*

SCORE	NO. OF CASES	PER CENT
45	4	0.7
46-55	39	6.4
56-60	78	12.8
61-65	137	22.5
66-70	171	28.1
71-75	106	17.4
76-80	42	6.9
81-90	25	4.1
91-100	7	1.2
Total	609	

iod of recovery may appear to be just as healthy as ever, but his dynamic fitness will be low, and unless it is tested, one can hardly accurately estimate his fitness.

SUMMARY

A brief report of the findings made at the initial health examination of 910 boys in the thirteen-to-nineteen-year age group is given.

The number of important and correctable defects made at such an examination even when the subjects come from an economically privileged group indicates the desirability of this sort of examination for all adolescents.

The importance of including an estimate of the functional fitness of a subject as well as observations made on him at rest is suggested.

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THE NUTRITIONAL BACKGROUND OF PATIENTS WITH RHEUMATOID ARTHRITIS*

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FOR a number of years the medical profession has come to believe with increasing conviction that the health of normal people is determined considerably by the type of food they eat, and that this has been proved to be of specific importance in certain diseases. A revolution is taking place in the practice of medicine at the present time because of this added information regarding nutritional requirements, and with more knowledge of objective evidences of deficiency states, patients are being found in clinics and offices whose symptoms and signs point to these states as the cause of their difficulties. It is becoming a more routine procedure to look into the patient's dietary history, evaluating the absorption of his diet and estimating his dietary requirements.

It is natural that this knowledge should be applied to chronic diseases of unknown etiology, and as the result of such studies, rickets, scurvy, beriberi and pellagra are no longer considered infections but are ranked as deficiency states. Pernicious anemia is known to be due to lack of an absorbed food factor, and certain neurologic conditions are responding to vitamin therapy. Acute deficiency states have been more easily recognized than are chronic borderline ones, and the possibility that borderline deficiency over a long period of time can cause certain diseases of unknown etiology is being kept in mind. Recently, a thorough study of the vitamin B complex therapy and the life history of cirrhosis of the liver has suggested that this disease of unknown etiology may be added to the list of diseases due to an incomplete diet.¹

Students of arthritis have not been slow in considering the possibility that food deficiency plays a role in the types of this disease whose etiology is unknown, but at the present time there is no proof that a lack of any specific food is a causative factor. The present belief that rheumatoid arthritis is of infectious etiology has led many to conclude that the evidences of a food deficiency

state that are often found are secondary to the disease. Indeed, this type of study was prompted by finding the red, smooth tongue and skin changes of vitamin B complex deficiency in a large number of patients with rheumatoid arthritis. In any event, work²⁻⁴ has been done that shows that these patients commonly have a deficiency in certain dietary elements. An increasing number of physicians⁵ believe that this food deficiency state should be treated with a well rounded and adequate diet, and that when it is so treated the general health of the patient usually improves, and at times coincidentally the disease itself.

Investigations of the diet of patients with rheumatoid arthritis have been numerous and revealing.⁶⁻¹² On the whole, they have established the fact that many of the food elements important in a well balanced diet are lacking, but they have failed in most cases to evaluate the dietary history of the patient at the period in his life previous to the onset of disease. One of us (F. C. H.) attempted this some years ago, but he failed to pay sufficient attention to the patient's absorption of food or to his apparent requirements for certain food factors. In some patients severe dieting for obesity, chronic hyperperistalsis and burning the candle at both ends have been conspicuous in the histories just prior to the onset of the arthritis. A high carbohydrate diet with evidence in the stools of starch indigestion has been observed in patients with rheumatoid arthritis.¹² Our recent observations appeared to show that 37 per cent of 40 patients with this type of arthritis had borderline or deficient diets prior to the onset of the disease. With recognition of the presence of food deficiency states, further study of their nutritional histories seemed important.

The remarks by Castle and Minot¹³ on the dietary history in anemia are applicable in this study of the dietary antecedents of rheumatoid arthritis. They say

It is important to emphasize to the patient that it is a description of the diet anteceding the present illness by months or years that is wanted and that it is what the patient himself eats, not the family as a whole which is the essential information. A detailed statement of the food taken at each meal in the day together with a statement of the number of times per day, week or month that the articles mentioned are eaten and approximately what amounts is a time consuming but necessary feature of the diet history.

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This has been our purpose in this paper. We have tried to evaluate and measure accurately the dietary background of our patients for the year before onset of their rheumatoid arthritis.

MATERIAL AND METHODS

Fifty-three patients with rheumatoid arthritis on the charity wards of the Robert Breck Brigham Hospital were interviewed and questioned concerning their dietary history by the method outlined below. The diagnosis of rheumatoid arthritis was confirmed in each case by clinical, roentgenographic and laboratory studies. Of these histories, those of 22 patients were discarded because of language difficulty, obvious memory faults and failure of the history to withstand rigorous cross-checking, leaving 31 cases for dietary analysis. Some of these patients showed evidence of avitaminosis on the skin or tongue.

Since our attempt was being made to evaluate the dietary history for the year before the onset of rheumatoid arthritis, the first questions were designed to date and describe the first symptoms that related to the disease process. The actual date of onset was set arbitrarily as the time that the patient noticed actual joint swelling. This determination was more difficult in the patients with the Strümpell-Marie variety of rheumatoid arthritis than in the others, but here steady pain or stiffness of the back was used as the criterion.

When the history of the year before onset had been obtained, brief descriptions of infections, operations, pregnancies and hyperthyroid states were elicited. Since these conditions definitely increase the calorie and vitamin requirement, their temporal relation to the year before onset must be known. Further questioning revealed factors that probably affected the total calorie and vitamin requirement. These questions concerned occupation, past and present, working and sleeping hours, duration of hours of relaxation and the way in which these hours had been spent. It was thought that the patient's race, birthplace, residence, marital, social and economic states and eating habits—whether he ate at home or in restaurants alone or with his family—all had some bearing on the total intake and requirement. Simple questions designed to reveal conscious or unconscious emotional strain and fatigue were asked. The total requirement before onset was evaluated on the basis of the answers to the above questions and of the age, height and weight at the time under consideration. This figure was given a percentile value, using 100 as normal.

Absorption of the food substances in the diet was largely evaluated on the basis of number and

character of stools per day and the use of cathartics and enemas to produce increased peristalsis.

The dietary history began with the meals of childhood and ended with the food eaten on the day before admission. Special attention was given to information that might by similarity or contrast shed light on the dietary customs of the prearthritic years. The intake of a hypothetical day during this period and also that during one or more different periods were recorded. In every case the information about the most clearly remembered time was checked and amplified by a detailed account of the estimated quantities of each of the fifty foods and beverages on a selected list that might be consumed in an average week. Special diets, prescribed or self-imposed, were listed and sometimes computed. The differences and similarities between the various periods were constantly stressed.

It was assumed that one seventh of an average week's intake should approximate, quantitatively and qualitatively, the corresponding typical day's intake. When this did not occur, the patient's accuracy was doubted. (In order to obtain a more logical picture the information about corresponding days and weeks was sought in separate interviews.) The history was considered inaccurate if the results of the computation of the diet seemed to disagree with the impression given by the patient, or if any of the figures for the two periods or for any period were too bizarre to be probable under the given circumstances. This rigorous cross-checking eliminated the majority of histories that were discarded.

The patient was asked to describe his appetite at different times by a single adjective. Brief inquiries into symptoms of allergy and indigestion were made. Prominent likes and dislikes of food were noted. Spontaneous comments on any of these topics were encouraged, as were comparisons of the patient's food habits with those of other people. Indications of strong feelings or parental attitudes on questions of diet were indirectly sought and noted.

The relative quantities of food contained in home-cooked meals were described by the patients in terms of hospital-diet servings, whereas restaurants were assumed to provide generally accepted averages. When several varieties of food were grouped under a single heading, such as "vegetable other than potato" or "cooked fruits," the available figures for those commonly used were averaged. Many similar compromises were made in estimating the food values of typical days, thus decreasing the distortion possible from the chance inclusion of some single high-vitamin food.

The composition and caloric content of the diets were estimated from charts giving data on the edible portion of uncooked food.¹⁴ The figures used for calcium, iron, thiamine, riboflavin and vitamin A were also estimated from values for un-

thrictic history seem to demand consideration. Such factors as trauma, infection, exposure, operations, increased activity, loss of weight, loss of appetite and increased nervousness did not appear to precede the arthritis in more than a small percentage

FIGURE 1. Summary of Data.

CASE No.	AGE	SEX	ENERGY	PROTEIN	CARBOHYDRATE	FAT	IRON	CALCIUM	VITAMIN A	THIAMINE	RIBOFLAVIN	VITAMIN C	THIAMINE/NOX FATTY CALORIES	TOTAL RE-QUE-MENT	DAILY
	yr.		cal	gm	gm	gm	mg	gm	int units	mg	mg	mg	ratio	%	%
<i>Rheumatoid arthritis</i>															
1	18	F	2071	60	223	105	12	0.6	4695	0.6	1.3	23	0.5	110	110
2	61	F	1378	54	156	59	14	0.3	8465	0.8	1.1	23	0.9	100	100
3	14	F	2786	108	287	132	20	1.2	9191	1.4	2.7	82	0.9	115	100
4	13	F	3019	99	365	126	15	1.3	5463	1.0	2.5	49	0.6	100	100
5	18	F	2691	75	364	100	14	0.3	3223	0.7	1.2	47	0.4	110	100
6	29	F	1599	65	161	77	10	0.8	6649	0.6	2.1	67	0.7	105	100
7	31	F	1899	60	161	112	20	1.6	31648	1.4	1.5	114	1.3	120	100
8	29	F	1690	66	176	80	14	0.6	8804	0.9	1.8	99	0.9	120	100
9	51	F	1688	52	196	77	10	0.7	7742	0.6	1.4	23	0.6	110	100
10	14	F	2229	75	265	95	13	1.2	4005	1.0	1.9	73	0.7	100	90
11	16	F	1907	70	237	75	13	0.7	3390	1.0	1.6	25	0.8	100	100
12	28	F	1584	54	151	84	8	0.3	3056	0.5	0.9	8	0.6	110	100
13	58	F	1663	69	156	84	14	0.8	6445	1.4	2.0	161	1.5	100	95
14	47	F	1826	51	300	46	8	0.7	5025	0.7	1.2	13	0.5	115	100
15	31	F	1640	60	200	70	12	0.9	5508	0.9	1.4	61	0.9	140	90
16	16	F	1923	61	219	90	9	0.6	5102	0.6	1.0	45	0.5	100	100
17	39	F	3058	108	419	105	20	0.6	4737	1.3	2.0	120	0.6	110	100
18	34	F	2720	79	321	119	15	0.6	7876	1.1	1.7	91	0.8	115	100
19	54	M	1697	74	180	77	13	0.4	6444	1.0	1.7	34	0.8	115	100
20	47	M	3861	115	362	216	16	0.3	2715	2.4	1.8	22	1.2	110	100
21	30	M	3711	163	417	155	26	0.9	4622	1.4	2.4	23	0.6	105	100
22	48	M	2795	109	322	118	24	0.4	8280	1.6	1.9	138	1.0	110	90
23	32	M	2345	83	215	128	17	0.7	7385	1.0	1.7	35	0.8	125	100
24	52	M	3758	118	426	158	19	0.4	57375	1.3	1.4	72	0.6	120	100
25	50	M	3435	96	470	129	19	0.4	5295	1.4	1.4	75	0.6	100	100
26	54	M	2117	56	256	96	12	0.4	7878	1.0	1.2	152	0.8	115	95
<i>Strömpell-Marie arthritis</i>															
27	32	M	3626	98	476	146	15	0.4	7440	1.4	1.3	23	0.6	110	95
28	26	M	2547	93	259	126	15	0.4	4076	0.9	1.5	16	0.6	120	100
29	24	M	3410	92	437	137	19	0.5	8225	1.1	1.5	45	0.5	120	90
30	21	M	2960	104	290	153	16	1.1	6445	1.1	2.6	45	0.8	110	100
31	15	M	3484	112	398	161	16	1.0	6580	1.3	2.5	75	0.6	125	100
<i>Families in North Atlantic cities*</i>															
\$125-187			2530	64			11.3	0.44	2100	1.0	1.2	41			
\$250-312			3320	88			15.4	0.65	3400	1.5	1.8	70			
<i>Recommended daily allowances for specific nutrients†</i>															
Man (70 kg.)			2500	70			12	0.8	5000	1.5	2.2	75			
			4500	70			12	0.8	5000	2.3	3.3	75			
Woman (56 kg.)			2100	60			12	0.8	5000	1.2	1.8	70			
			3900	60			12	0.8	5000	1.8	2.7	70			

*These figures show the nutritive values per nutrition requirement unit—equivalent to the daily allowance for a moderately active man weighing 154 pounds (70 kg.)—for diets of families at different 1936 price levels per person per week. These averages refer to food brought into the kitchen and take no account of the edible food waste or nutritive losses resulting from cooking.¹⁴

†These figures are taken from a table¹⁵ that presents a tentative goal toward which to aim in planning good diets for normal people at different levels of age and physical activity. The values refer to the amount of each factor to be eaten.

cooked foods, but deductions of 30 and 35 per cent, respectively, were made to allow for the thiamine lost in cooking vegetables and meats.¹⁵ The vitamin C figures were taken from a table that included analyses of foods subjected to various processes, such as storage, cooking and reheating.¹⁶ Other recognized sources were consulted in the few cases in which these did not yield the required information.

RESULTS

Table 1 presents the quantitative data obtained in this study. Certain features of the general ar-

thritic history seem to demand consideration. Such factors as trauma, infection, exposure, operations, increased activity, loss of weight, loss of appetite and increased nervousness did not appear to precede the arthritis in more than a small percentage of cases. On the other hand, 12 patients gave histories of skeletal or muscular pain that had persisted or recurred for one month to several years before the first joint swelling considered the actual onset of arthritis. Nine patients described changes in physical vigor that preceded the arthritis by one month to three years. Six patients thought there had been a one-year or two-year period of increased emotional strain before the onset. In 10 cases, changes in home, school or working conditions seemed to bear a temporal relation to these variously diagnosed symptoms. Of the 5 patients who had pregnancies within

three years before the onset of arthritis, 3 failed to recover their previously good health. Although 8 patients said that they had been constipated for years or always, none thought that this had increased in the year before onset. It is interesting that none of this group complained of diarrhea — but they did use cathartics freely.

In evaluating the factors in the diet, we have compared our findings with three sets of standards: first, when possible, with actual requirements as mentioned by various authors to be quoted; second, with the average American diet in North Atlantic cities¹⁷; and third, with the recommendations of the National Research Council for an optimal diet.¹⁸ The results, evaluated by these three standards, are as follows:

Calories. The criterion for energy requirement was met by maintenance of normal body weight. The 4 patients who lost weight were considered to have had too few calories. Three patients gained weight. The average intake was 2712 calories, with the wide range of 1378 to 3758 calories. In their study of present-day diets in the United States, Stiebling and Coons¹⁷ found average daily caloric intakes of 2530 and 3320 at different price levels among families in cities of the North Atlantic states.

Protein. The average protein requirement of a 70-kilogram man has been stated to be 44.4 gm. daily, and it is customary to allow from 10 to 15 per cent of the total calories for protein.¹⁵ The average daily protein intake in our series was 84 gm., and single diets contained from 51 to 163 gm., accounting for 10 to 17 per cent of the total calories. There was no intake below 44.4 gm. Four females had questionably low protein intakes of less than 55 gm., but the general average was higher than those of 64 and 88 gm. found by Stiebling and Coons.¹⁷ Nine females and 1 male had less than the absolute quantity recommended by the National Research Council,¹⁸ but none of these were inferior to this recommendation in their ratio of protein to total calories.

Carbohydrate. A daily average of 286 gm. of carbohydrate, with a range of 151 to 476 gm., or 34 to 66 per cent of the total calories, was found in the diets. In only 6 of these did carbohydrates appear to have accounted for more than 50 per cent of the calories. This was an unexpected finding, since it is generally believed that patients with rheumatoid arthritis use a high-carbohydrate diet.

Fats. The average daily fat intake was 112 gm., with a range of 46 to 216 gm., or 24 to 53 per cent of the total calories. This was not very different from the average in the United States,

where it is generally accepted that about one third of the food calories are taken in the form of fat.¹⁵ If anything, the intake was high in this respect, since 16 patients took over 40 per cent of their calories in the form of fat.

Iron. The estimated iron need of the normal man or woman is 8 mg. daily.¹⁵ Our patients had an average of 15 mg. (females 13.4 mg., males 17.5 mg.), with a range of 8 to 26 mg. Three women, however, took less than 10 mg. daily. One of these was sixteen years old and obviously should have had more iron. Stiebling and Coons¹⁷ found average iron intakes of 11.3 and 15.4 mg. for two economic groups. Although all our patients apparently met their actual requirements, 7 women had less than the National Research Council's¹⁸ recommendation for their age group.

Calcium. The normal requirement for adults is probably a little over one hundredth of the protein requirement, or approximately 0.45 gm. daily, whereas the present standard of adequacy for those who have not reached full skeletal growth is 1.0 gm.¹⁵ Our patients had diets containing 0.27 to 1.60 gm., with an average of 0.7 gm. Twelve had less than one hundredth as much calcium as their protein requirement. An eighteen-year-old girl had less than one third of the standard amount thought needed during growth. Three other girls under twenty years of age had distinctly less than 1 gm. Three men with rheumatoid arthritis had 50 per cent of their estimated requirement, and 1 had only 36 per cent. Three men with Strümpell-Marie arthritis had less than their requirement, 1 of them by over 50 per cent. However, this evidence of low calcium intake is also found in other American diets. Stiebling and Coons¹⁷ found averages of 0.44 and 0.65 gm. in their two groups, and Sherman¹⁵ found a range of 0.24 to 1.87 gm., with an average of 0.73 gm., in the one hundred and fifty families included in his study. The recommendations of the National Research Council¹⁸ were met by only 4 females and 2 males.

Vitamin A. Computation of the vitamin A value gave results ranging from 2715 to 9193 international units, or much higher if vitamin supplements were included. Although vitamin A content cannot be judged with any precision, probably no patient had as little as 1750 international units, which is the lowest requirement figure for a person weighing 70 kilograms.¹⁵ Stiebling and Coons¹⁷ suggested that the 2100 and 3400 international units of vitamin A value given in the diets studied by them might be too low.¹⁷ Although the average of the diets in our group (omitting supplements) was around 6000

international units, 7 females and 3 males had less than the amounts in the National Research Council's¹⁸ table.*

Thiamine. The thiamine requirement may be stated in terms of the ration between micrograms of thiamine and non-fat calories.¹⁵ The average ratio necessary to protect against beriberi is 0.3.¹⁹ The thiamine nonfat calorie ratio in our patients averaged 0.8, ranging from 0.4 to 1.5. The average thiamine intake was 1.0 mg. and the range was from 0.4 to 2.4 mg. daily. Stiebling and Coons¹⁷ found averages of 340 and 500 international units or 1.0 and 1.5 mg. (with no allowance for cooking losses) in the diets they studied. The National Research Council¹⁸ recommends more thiamine than was found in the diets of our patients with the exception of 4 females and 2 males with rheumatoid arthritis; since, however, the allowances for thiamine are proportional to total calories, quantitative comparisons with diets high in fat may be misleading.

Riboflavin. The minimum daily riboflavin requirement proposed for adults is 1.0 mg.¹⁵ Our patients had from 0.9 to 2.7 mg., with an average of 1.7 mg. Eight patients, 6 of them females, had between 0.9 and 1.3 mg. Stiebling and Coons¹⁷ found averages of 470 and 700 international units (1.2 and 1.8 mg.). Although the average of riboflavin in our patients' diets was apparently as good as or better than that in the average American diet, only 10 patients met the standards of the National Research Council.¹⁸ Seven out of 8 male patients with rheumatoid arthritis and 3 males with Strümpell-Marie arthritis had considerably less than this recommendation and it was met by only 7 females.

Vitamin C. The vitamin C requirement of adults is stated to be 1.0 mg. per 100 total food calories, or about 25 mg. daily.¹⁵ The intake of patients with rheumatoid arthritis averaged 62 mg. and ranged from 8 to 161 mg., or from slightly more than one half to ten times the requirement in relation to the number of total calories. Eight patients had intakes of less than 25 mg. and 8 had between 25 and 50 mg. in their daily diet. In definite contrast were several high vitamin C intakes (114, 120, 138, 152 and 161 mg.). Stiebling and Coons,¹⁷ calculating the ascorbic acid content of the uncooked foods of families in North Atlantic cities, found averages of 41 and 70 mg. per person. Again, as compared to the National Research Council's¹⁸

recommendations, 11 females and 3 males with rheumatoid arthritis were deficient in vitamin C. None of the patients with Strümpell-Marie arthritis had as much as the allowance for their ages.

COMMENT

Studies of the diet and nutritional status of patients with rheumatoid arthritis have revealed many deficiencies in intake and a lack of vital foodstuffs that can be observed in patients or measured in the chemical laboratory.²⁻¹² The present survey indicates that the dietary history of these patients before onset is not grossly different from that of a cross section of employed families in the North Atlantic states.¹⁷ However, over two thirds of the patients fell short of the National Research Council's¹⁸ recommendation for calcium, thiamine and riboflavin; about half had an inadequate intake of vitamin C, and a small number were deficient in protein, iron or vitamin A or its precursors by the standards set by this council.

These facts seem to be of great significance until it is realized that in terms of actual requirement only a few patients gave a history of an abnormal foodstuff intake that would lead to obvious clinical deficiency states, and that then only calcium and vitamin C were involved. The rather high incidence of signs, symptoms and laboratory findings of food-deficiency states observed in groups of patients such as these should be ascribed to a deficiency resulting during the course of the disease or to an essentially normal dietary background that has been made relatively insufficient by abnormal requirement caused by such factors as increased work, worry and chronic fatigue.

The analysis of this series indicates that the greatest tendency toward deficiency lay in the requirement background of the patients rather than in the actual food consumed. All but 7 had unusual expenditures of nervous or physical energy prior to the onset of disease, and this produced the same result that faulty food intake would have produced.

The etiologic factor or factors involved in rheumatoid arthritis are still to be elucidated, but from this study it seems apparent that if a food factor contributes to the onset of this disease process, its lack is brought about by an increased requirement rather than by a deficiency in intake. The results of the study do not invalidate the evidence for definite food deficiency in individual patients with rheumatoid arthritis; they only indicate that the dietary background of the patients studied is within average limits. Until patients can be studied before onset of the disease it must

*A note on this table adds that requirements may be less if vitamin A is provided as such and if it is chiefly provided as the pro-vitamin carotene.

be assumed that the food-deficiency state is probably secondary to the disease.

SUMMARY AND CONCLUSIONS

The dietary history of 31 patients with rheumatoid arthritis was reviewed for the year before the definite onset of their disease process. This history appeared to show that the food intake was essentially the same as that of a cross section of families in the North Atlantic states. The intake of calories, protein, fat, carbohydrates, vitamin A and its precursors, thiamine, riboflavin, vitamin C, calcium and iron was studied.

If a food-factor deficiency contributes to the onset of rheumatoid arthritis this study suggests that it must be caused by an increased total requirement of the patient rather than in a deficiency in his average diet. In single cases a deficient diet may be found to have been present prior to the onset of the disease. It should always be looked for and corrected when found. The very frequency of evidences of deficiency states during active rheumatoid arthritis suggests that this disease increases the food requirements, especially of the vitamin B complex.

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MEDICAL PROGRESS

ADVANCES IN MALARIA RESEARCH (Concluded)

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IMMUNITY

SIGNIFICANT recent advances have been added to the knowledge of immunity in malaria. Immunity in this infection has been little understood, and even questioned, but the results achieved within recent years offer encouragement and methods of approach for an eventual solution of unsolved problems. An understanding of the newer available knowledge is of particular importance to the clinician and epidemiologist who are called on to treat and study the occurrence, spread and control of this disease.

Extensive studies with human malaria, particularly induced malaria, have definitely proved that patients acquire immunity during the course of an infection. James in England, Ciuca in Rumania and Boyd and his collaborators in America

and others have helped to explain race susceptibility to malaria, and the development of immunity not to a species of *Plasmodium* but to strains or races of each species. The immunity that is acquired is highly effective against reinfection with the homologous strain, but fails to protect against heterologous strains and species of parasites.

This discovery of different strains within a species helps to explain the resistance or tolerance of a given population to the local strains, the length of time it takes the effective immunity to develop susceptibility to foreign strains, the variable clinical activity observed for different strains of the same species and finally the variable response to antimalarial drugs. James and Ciuca¹ cite the work of Korteveg, who compared two strains of *Plasmodium vivax*, one from Holland and the other from Madagascar. Infection with the Holland strain remained latent in 38 per cent of cases; there was an average incubation period of twenty-one days, giving 19 per cent with quo-

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tidian paroxysm, 8 per cent with fever above 106.4° F., 10 per cent with spontaneous recovery and 10 per cent with relapses and a high resistance to neosalvarsan. The Madagascar strain was a much more virulent one, with 7 per cent latency, an incubation period of twelve days, 80 per cent with a quotidian paroxysm, 30 per cent with fever over 106.4° F., no spontaneous recoveries, a relapse rate of 80 per cent and high susceptibility to neosalvarsan. DeBuck (also cited by James and Ciuca) found that the Holland strain produced an average number of 13 merozoites (range 8 to 20) while the mean in the Madagascar strain was 18 (range 8 to 32). Furthermore, immunity acquired against the Madagascar strain did not protect against the Holland strain.

James, Nicol and Shute⁷⁹ compared strains of *P. falciparum* from Rome and India. Clinically, the strain from Rome produced severe disease and even several cases of blackwater fever, in contrast to mild attacks from the Indian strain. *Anopheles maculipennis* could be infected with the Italian but not with the Indian strain. Furthermore, patients recovering from attacks caused by the Indian strain were susceptible when reinoculated with the Roman strain. Boyd and his collaborators⁸⁰⁻⁸² conducted similar studies with American strains of *P. vivax* and *P. falciparum*. They found clinical and immunologic differences between strains, and also differences in their ability to infect anopheline vectors.

Homologous immunity develops to strains of *P. malariae*, but variations between strains of *P. ovale* are not yet clear. The only case of cross or heterologous immunity between species infective for human beings exists for *P. vivax* in patients recovering from infections with the simian parasite *P. knowlesi*,¹⁷ but Milam and Kusch⁸³ failed to demonstrate the reverse.

Two approaches have been used to elaborate the mechanism involved in natural and acquired immunity. Cellular reactions to various types of malaria have been carefully studied, and standard immunologic methods have been utilized in investigating humoral response to infection.

Observations on phagocytosis of parasitized red cells, extracorporeal parasites and pigment in malaria began with the early, thorough and brilliant observations of Laveran and Golgi, and represent the most consistent findings in the pathological literature of this disease. The extensive work of Cannon and Taliaferro,⁸¹ Taliaferro and Cannon⁸⁵ and Taliaferro and Mulligan⁸⁶ has clarified experimentally the sequence of events in avian and simian malaria.

Defense against the infection depends on the response of the lymphoid-macrophage system. The process of phagocytosis takes place primarily in the spleen, with decreasing activity in the liver and bone marrow. Natural immunity to the infection is evidenced during the early days of the infection by a relatively small amount of phagocytosis. During and after the crisis, the phagocytic activity is greatly increased and is associated with proliferation of macrophages. This initial response requires time for mobilization in nonimmune animals, but the response after superinfection is very rapid in animals with acquired immunity. The proliferation of lymphoid-macrophage tissue in the spleen offers a basis for splenomegaly or the progressive increase in size of this organ during the course of the disease. This cellular defense is active only against the strain or race of parasite that caused the infection. With each new infection, the same sequence of events appears to be necessary in order to build up cellular defense.

The greater susceptibility of children to malaria indicates either that more time is necessary to acquire effective immunity or that the defense mechanism in children is not so efficient as that in adults. Many workers have shown that the incidence of clinical malaria begins to decline at two to five years and drops rapidly to sixteen years and over, even though high parasite and splenic rates persist. Apparently this type of immunity is immunity against clinical symptoms, not parasites, and depends on the persistence of parasites in the subject. In fact, the terms "premunition"⁸⁷⁻⁸⁹ and "infection immunity"⁹⁰ were coined to differentiate the type of immunity in malaria from that in which the infection has subsided and the causative organism is no longer present. There is evidence, however, that acquired immunity may persist for three and a half to five years after the initial attack, without the persistence of parasites in the tissues. These cases were adequately controlled by subinoculating normal persons with large quantities of blood. On the other hand, malaria, particularly quartan malaria, may remain latent for twenty years or more and infect a normal person when blood is given for transfusion.^{91, 92}

Early attempts were made to demonstrate the therapeutic value of immune serum in malaria.⁹³⁻⁹⁵ The qualitative and quantitative demonstration of passive immunity by Coggeshall and Kumm⁹⁶ showed conclusively that protective antibodies are present in the circulating blood of monkeys with chronic malaria. Later the more potent effect of hyperimmune serum produced by superinfection was shown.⁹⁷

As previously mentioned, complement-fixing antibodies^{25, 26} and agglutinins³⁰ were demonstrat-

ed in monkey malaria, *P. knowlesi* being used as an antigen in both cases. The complement-fixation reaction became positive promptly after an acute attack and then dropped slowly, to rise again after a relapse. The titers varied from monkey to monkey, but with no relation to the parasite index. Serums giving high titers did not always confer high protection in the experiments on passive immunity. The reaction was later used to test serums from cases of induced human malaria with *P. knowlesi*, *P. vivax* and *P. falciparum*, and from naturally acquired tertian and malignant tertian malaria. The interesting and important results of this work showed that the reaction was group specific and not species specific and, furthermore, that the reaction with *P. knowlesi* as an antigen had a practical application to the diagnosis of human malaria.

The work of Dulaney and Stratman-Thomas²⁷ and Dulaney, Stratman-Thomas and Warr²⁹ on serums from naturally acquired and induced human malaria, and that of Kligler and Yoeli²⁸ on serums from malaria in a hyperendemic area, demonstrate that the test is specific and reliable and of practical value. Technical difficulties, however, make the reaction a supplementary test to the simpler and easier routine blood examinations. Another interesting discovery was the failure of pre-existing syphilis to interfere with the specificity of the reaction. When the syphilitic reagin is absorbed out of serums from a syphilitic and malarious patient, the serum reacts as before for complement-fixing antibodies. The reverse is not true, for it is well known that serums from patients with malaria give false-positive Wassermann and Kahn reactions.⁹⁸ These reactions exist for variable times during and after clinical malaria, showing that malaria must be ruled out in a patient from an endemic malarious area before he is given treatment for syphilis.

The agglutination reaction in simian malaria was found to be species specific by Eaton. Because of difficulties in obtaining suitable human antigen, the test is of little practical value for diagnostic purposes. An interesting finding that may have more bearing on the slow antibody response was the failure to obtain agglutination of red cells containing immature parasites. Perhaps the limited time that the mature intracorporeal parasites and extracorporeal merozoites from segmentation can act as antigens explains the relatively slow development of immunity.

The highly specific agglutination reaction of sporozoites when the infected salivary glands of mosquitoes are dissected in homologous immune serum is a more recent development that may be of far-reaching importance. This phenomenon

was originally observed in 1900 by Stephen and Christophers cited by Mulligan and Russell.³¹ Mulligan, Russell and Mohan,³² using *P. gallinaceum* of chicken or fowl malaria, obtained agglutination in dilutions ranging from 1:1000 to 1:65,000. When wild infected mosquitoes were dissected in human serums from chronic cases of malaria in the same locality, sporozoites agglutinated in dilutions of 1:4000 and 1:8000. In these same human immune serums, sporozoites of *P. gallinaceum* agglutinated only in dilutions of 1:128. Thus, agglutination of sporozoites appears to be highly specific and sensitive to humoral antibodies. Whether or not the procedure can be used for the diagnosis of human malaria will depend on the development of methods for rearing and maintaining a constant supply of heavily infected mosquitoes.

Russell, Mulligan and Mohan⁹⁹ tested the agglutinogenic effect of sporozoites of *P. gallinaceum* inactivated by ultraviolet light. A higher agglutinating titer was obtained in this way than by blood inoculation of the homologous plasmodium. An agglutinating titer of 1:32,000 or higher lowered the mortality rate from 51.4 to 7.7 per cent. When fowl immunized against sporozoites were inoculated with homologous trophozoites, no protection was detected.¹⁰⁰ In a later series of experiments by Russell and Mohan,¹⁰¹ vaccinations with inactivated sporozoites, injections of homologous immune serums and combinations of both vaccine and serum gave mortality rates of 21.1 per cent, 16.7 per cent and 7.3 per cent, respectively. The incubation time was not affected, but the intensity of infection was lowered. Since the greatest prophylactic effect was obtained in the third series, these authors believe that there is a combined action of humoral and cellular mechanisms in defense against malaria.

A successful precipitin test has been developed,³³ with use of an extract of infected placenta for the antigen. The scarcity of such antigenic material has prevented the adoption of the procedure. Stratman-Thomas and Dulaney³⁰ were unable to get positive results with antigens made from human blood. Dulaney and House,³⁴ however, have been able to get precipitative reactions in human malaria with an antigen of *P. knowlesi* using the collodion-agglutination technic of Cannon and Marshall³⁵ and the collodion-fixation procedure of Goodner.³⁶ Since these methods were found by their original authors to be highly sensitive when compared to the standard precipitin reaction, they appear to be the methods of choice also for human malaria.

When one attempts to correlate the above findings, it is pertinent to recall the provisional theory that Welch¹⁰² proposed in 1897 to explain what

he termed natural resistance to the malarial parasite—a theory similar to that accepted regarding resistance to bacteria. He postulated that . . .

. . . the parasites are destroyed by parasitocidal substances both in the plasma and within leukocytes and other phagocytic cells. The substances injurious to the parasites are in the last analysis furnished to the plasma by the cells and are in a more concentrated or potent form within the cells than in the fluids. This theory assigns to the phagocytes a higher role than that of mere scavengers. They are endowed in especial degree with the power of destroying the parasites, but this power is shared by the plasma.

Smith¹⁰³ also suggested that malarial immunity may reside both in the blood and in the host cells themselves.

The theory of Welch and the suggestion of Smith now appear to be correct, for available information suggests that cellular and humoral immunity do not work independently, but combine to aid the host in defense. The experimental evidence supports this view. The results of Russell and Mohan¹⁰¹ have already been cited, but the work of Mulligan, Sommerville and Swaminath¹⁰⁴ also confirms this opinion. In simian malaria, immune serum failed to affect the course of the disease in splenectomized monkeys. Furthermore, the enhanced value of immune serum in treating infections with *P. knowlesi* depended on the degree of stimulation of the lymphoid-macrophage system caused by the previous injection of another species of parasite (*P. cynomolgi*). The determination of more definite and precise relations between cellular and humoral mechanisms in defense against malaria will have to await the results of correlated quantitative studies on the cellular response and circulating antibodies.

In the foregoing account, the evidence for cellular defense and protective antibodies in malaria has been briefly reviewed. The studies demonstrate the slow but gradual increase in the development of acquired immunity. When the course of the infection has been interrupted by immediate treatment, the formation of antibodies is prevented and hence no immunity is acquired. One can readily see that here is the basis for the frequent observation in a native population that a "seasoning process" to malarial paroxysms is necessary before beginning treatment. Thus, the experimental results of recent years give credence to the above observation learned by experience in malarious areas.

Assuming the variation of specific antigenicity and host response under extreme conditions of climate and malnutrition, the level of immunity or activation of the lymphoid-macrophage system

and production of protective antibodies is entirely dependent on the intensity and duration of the infection. Short-lived infections produce little or no immunity. In long-standing chronic infections, a high grade of immunity is acquired. Observations on the potency of immune serum, the development of humoral antibodies and cellular defense support the statements.

Thus, Sinton,¹⁰⁵ who has compared his results of treatment on the development of immunity in simian malaria (*P. knowlesi*) with observations by other workers on the treatment of human malaria, points out that circumstances should determine the aim of the practitioner in the treatment of malaria. If there is little chance of reinfection, attempts should be made to effect a radical cure with suitable antimalarial drugs. If radical cure is not achieved and a relapse develops at a later date, the patient should undergo series of paroxysms before treatment is resumed. If such a procedure is to be carried out successfully and without fatalities in patients relapsing with *P. falciparum*, the blood must be examined daily to follow the parasite density and treatment must be resumed if the concentration of parasites approaches a dangerous level (100,000 per cubic millimeter).¹⁰⁶ If patients appearing for treatment are constantly exposed to reinfection, radical cure should not be attempted but rather a rapid cure of clinical symptoms only. There is ample evidence of the higher morbidity and mortality rates in endemic and hyperendemic areas where radical cures rather than clinical ones are attempted. The persistence of low-grade infections helps to maintain and even build up effective immunity against the local strains of parasites. The loss of immunity in a malarious area leads eventually to outbreaks of epidemic malaria.

TREATMENT

Advances in the treatment of malaria leave much to be hoped for and accomplished, since the ideal drug for malarial therapy has not been found. Despite the widespread incidence of malaria, there is no general agreement about the methods of treatment. Actually this situation is what one might expect when one considers the great variety of parasitic strains, the wide difference between benign tertian and malignant tertian malaria and in addition the effects of race susceptibility, acquired immunity, malnutrition and many other factors that make up the state of health of the human host in his environment.

Three antimalarial drugs have been tested and used successfully: the cinchona alkaloids, of which quinine is the best known, and two synthetic drugs, atabrine and plasmochin. Atabrine is the

only substitute for quinine, because plasmochin is useful only as an effective drug for the specific destruction of the gametocytes or sexual stages of malignant tertian malaria that lead to the infection of anopheline mosquitoes and transmission of the disease.

The loss to this country of the Netherlands East Indies has cut off the source of 90 per cent of the supply of quinine.¹⁰⁷ This fact has caused an emergency situation in view of the great need for antimalarial drugs for prophylaxis and treatment of great numbers of troops operating in endemic malarious areas. Thus, the War Production Board has frozen and restricted the use of all stocks of quinine and other cinchona alkaloids. Furthermore, the National Research Council undertook to investigate the available supply, use and standardization of cinchona bark from South America for the production of totaquine, a compound of cinchona alkaloids (quinine, quinidine, cinchonine and cinchonidine). Fortunately this compound was investigated by the League of Nations¹⁰⁸ some years ago and the results obtained from it were found to be more or less equivalent to those obtained by the use of quinine alone. Totaquine has now been recognized by the *Pharmacopoeia of the United States* and the definition appears in a supplement to the twelfth edition.

Until supplies of quinine and totaquine have been built up and made available, necessity forces the use of atabrine. The production of this synthetic drug has been greatly increased by the War Production Board, and presumably adequate supplies for all needs are available.

Here again, the League of Nations¹⁰⁹ conducted experiments on the relative prophylactic and therapeutic value of atabrine versus quinine. Patients with induced and naturally acquired malaria were used, and experiments to eradicate malaria were conducted. The experiments involved a total of 12,288 persons in five areas—Algeria, Italy (Sardinia), Federated Malay States, Rumania and the U.S.S.R. The studies of Clark et al.¹¹⁰ in Panama and of other workers in Africa and in India have also aided in assessing the therapeutic and prophylactic value of atabrine.

Atabrine is an effective prophylactic drug (except in hyperendemic areas) when two tablets (0.1 gm. or 1½ gr. each) are taken on two successive days each week. The recommendation by the British and American armies advises a two-day or three-day interval between days of medication.¹¹¹ A daily prophylactic dose of 0.06 gm. was the method used by the Germans in the Balkan campaign of the present war.¹¹² Daily prophylactic doses not exceeding 0.1 gm. are considered advisable for troops in hyperendemic areas where malignant tertian malaria is prevalent.¹¹³ The ac-

cepted dosage for clinical malaria is one tablet (0.1 gm.) three times a day for seven days. Since the drug is accumulative, an interval of seven to ten days should elapse before another course is given. In the treatment of acute malignant tertian malaria, Bryant¹¹⁴ used two to three times the accepted dosage profitably, giving sweet hot tea simultaneously to lessen the occurrence of toxic symptoms. For cases of acute malaria in adults, where rapid absorption is required to control symptoms, atabrine musonate* can be injected slowly intramuscularly (0.3 gm. in 10 cc. of distilled water divided into three daily doses) or intravenously (0.3 gm. in 20 cc. of a 10 per cent solution of glucose divided into three daily doses). There is no agreement about the route of choice.

Slight toxic effects—gastrointestinal disturbances, nervous and mental symptoms and yellow pigmentation of the skin—occur in a certain percentage of patients treated with atabrine, but these untoward effects are usually temporary and the yellow pigmentation is not the result of liver damage.¹⁰⁹ Toxic effects are more pronounced in children, and for this reason quinine is still the drug of choice in treating children up to five years of age. Junge¹¹⁵ has made some interesting observations in a report on the continuous use of atabrine for prophylaxis over a period of seven years. Twenty Europeans in Liberia were involved, and each subject took 143 gm. of atabrine in the elapsed time without injury to general health, even though yellow pigmentation was constant. The original daily dose of 0.1 gm. was cut to 0.05 gm., and no malaria developed in three and a half years. When the dosage was cut to 0.03 gm. daily, 16 persons came down with quartan or malignant tertian malaria, demonstrating that the effective prophylactic dosage was not less than 0.05 gm. daily.

The tendency of patients with malaria to relapse after treatment with quinine is characteristic. In a series of controlled experiments by various workers, the relapse rate after treatment with atabrine is slightly less than that after quinine.¹⁰⁹ There are still relapses, however, and so long as relapses occur after the use of any drug, transmission can take place if the anopheline vectors gain access to a blood meal containing gametocytes of the plasmodium. Furthermore, the following fact must be emphasized: atabrine has no effect on the gametocytes of *P. falciparum*, and patients with this type of malaria must be treated also with plasmochin.

Plasmochin has no value for the treatment of clinical malaria, according to various authors.

*In this country, atabrine dihydrochloride is usually employed. The intramuscular dose is 0.1 gm., dissolved in 3.5 cc. of distilled water, and the intravenous dose, 0.1 gm., dissolved in 10 cc. of distilled water, each given three times daily.

This drug has a definite effect on the gametocytes of the three species of malarial parasite, being especially effective against gametocytes or the "crescents" of *P. falciparum*. For this reason a course of the drug is given after quinine or atabrine to prevent transmission of malignant tertian malaria. The correct dose is 0.01 gm. (3/20 gr.) three times daily after meals for five days. The drug is highly toxic, and only 0.02 gm. per day should be given to a debilitated patient. Also, the drug should never be given at the same time as atabrine, because the two enhance the toxic symptoms of one another. This is not true, however, for quinine and atabrine, since Hill and Howie¹¹⁰ report the successful simultaneous use of quinine (10 gr. three times a day) and atabrine (1½ gr.) three times a day for seven days in treating 200 cases of malignant tertian malaria.

The combined or QAP treatment, used in India by Amy and Boyd¹¹⁷ and later by the British Army, has been endorsed by the Subcommittee on Tropical Diseases of the National Research Council.¹⁰⁷ This procedure is now considered the treatment of choice for acute malaria. Owing to its more rapid action in controlling the pyrexia and multiplication of parasites, quinine sulfate or totaquine (0.64 gm. or 10 gr.) is given three times a day for two or three days. Atabrine (0.1 gm. or 1½ gr.) is then given three times a day after meals for five days. After two days' rest from medication, plasmochin (0.01 gm. or 3/20 gr.) is given three times a day after meals for five days. For less serious cases, atabrine-and-plasmochin or quinine-and-plasmochin combinations are satisfactory.

Blackwater fever or hemoglobinuric fever, a disease that is connected with attacks of malaria or continuous malarial infection with *P. falciparum*, has not been considered above because of limited space. The treatment in brief consists of symptomatic relief, cessation in most cases of treatment with antimalarial drugs and administration of an alkali to render the urine alkaline within twenty-four hours after onset¹¹⁸; in acute cases, blood transfusions are decidedly helpful. No specific drugs for this disease are known. For a full account of blackwater fever and its treatment, the reader is referred to textbooks on tropical medicine.

Physicians or medical officers treating their first cases of malaria should be aware of the possibility of relapse after any known method of treatment and follow the patient accordingly. Furthermore, malaria may assume a great variety of clinical manifestations that are not commonly described in the typical textbook discussion. The same is true to some extent of response to treatment. Consequently, malaria in one of its many forms should be expected in a patient returning from an en-

demic malarious area until a thorough, accurate blood diagnosis establishes the absence of plasmodia. If patients with malaria are refractory to the usual methods of treatment, further information should be sought from more complete accounts on the therapeutics of malaria.^{9-11, 118-120}

The persistence of a low relapse rate in malaria after all known methods of treatment, and the failure of prophylaxis with quinine or atabrine to kill the infective sporozoites and prevent infection, have provided the stimuli for continued efforts to find new and more effective drugs. In fact, the war and its disastrous effect on our source of quinine has made studies in the chemotherapy of malaria one of the foremost and urgent fields of research. The approach to this pressing problem has been varied, and a colossal amount of work in preparing and testing new compounds has been and is being done.

Effort has been concentrated to a large extent on the quinoline and acridine compounds because of the antimalarial activity of the cinchona alkaloids, atabrine and plasmochin. The compounds prepared and tried are numerous. A thorough review of this subject and the general subject of chemotherapy of malaria has been compiled by Williams.¹²¹ The sulfonamides, including the well-known compounds and lesser-known derivatives, have been receiving increased attention.

The use of sulfonamide compounds in the treatment of malaria dates from the work of De Leon,¹²² who claimed to have treated 15 cases with Rubiazole successfully. This work and that of Hill and Goodwin¹²³ with Prontosil Soluble in this country have not been confirmed.¹²¹ The results obtained from sulfanilamide, sulfathiazole and sulfapyridine in simian malaria greatly stimulated research when the discovery was made that these drugs would sterilize infections of *P. knowlesi* in rhesus monkeys.¹²⁴⁻¹²⁷ However, sulfanilamide and sulfathiazole did not effect complete sterilization of simian infections with *P. inui* and *P. cynomolgi*.^{12, 128} Nevertheless, if these drugs proved to be effective in human malaria, they could be used to treat cases refractory to other antimalarial drugs and also exert bactericidal and parasitocidal action in complicated cases with pneumonia or other acute infections. Unfortunately, the results to date are not in agreement—a possible indication of low antimalarial activity. Sulfanilamide and Prontosil have not proved effectual. Sulfapyridine has a temporary effect on the parasites, but relapses soon occur.^{129, 130} Coggeshall, Maier and Best¹³¹ have obtained promising results with promin and sulfadiazine. The antimalarial activity of promin was first demonstrated in 5 patients with induced malaria. The drug was later tried on 17 patients with naturally acquired

malaria (12 with *P. vivax* and 5 with *P. falciparum* infection) in Panama. Patients with malignant tertian malaria responded better than those with tertian infections. This result is in keeping with the selective action noted with sulfonamides on simian malaria, and led the authors to assume that these drugs have the greatest effect on the more virulent infections. Sulfadiazine was used on 13 Negroes (7 infected with *P. vivax*, 5 with *P. falciparum* and 1 with *P. malariae*). The drug showed a definite effect in 10 cases but failed in 3. Thus, the authors demonstrated considerable antimalarial activity with promin and sulfadiazine, but only point out the need for more extensive trials and assert that these two drugs are not substitutes for quinine and atabrine.

In the experimental and field trials with sulfonamide drugs in malaria, one disturbing factor stands out. These drugs often show highly variable effects on different species of *Plasmodium* in man, monkeys and birds. One can foresee the possibility that an effective drug against human malaria may be overlooked if the testing is done with avian or simian malaria. Furthermore, Coggeshall and Maier⁷² failed to find that inhibition of respiration in vitro by drugs was an index of chemotherapeutic efficiency with five species of *Plasmodium*. Consequently, thorough testing of drugs with antimalarial activity must be conducted on human as well as avian or simian malaria in order properly to evaluate their effectiveness. Admittedly, human trials are difficult, but at least efforts can be made in this direction.

Great promise of a new type of antimalarial drug has resulted from the discovery that amidino compounds have significant activity against malaria¹³² as well as trypanosomiasis, leishmaniasis, and infections with *Babesia canis* in dogs.¹³³ The amidino compounds tested thus far include undecane diamidine in tertian malaria and 4:4-diamidino stilbene (Stilbamidine) in tertian and malignant tertian infections. These drugs had definite and effective antimalarial activity, but trials have been too few to evaluate. The parasitocidal, bacteriostatic and bactericidal activity of the drugs is being tested widely, and the results appear to be encouraging.

Arsenical compounds and a number of drugs containing bismuth have been used for antimalarial treatment, but they are generally of value in controlling paroxysms rather than as curative drugs for the destruction of the parasites. Arsphenamine, neoarsphenamine, tryparsamide and Mapharsen are the drugs containing arsenic that have received the most attention. From the data presented by Winckel,¹³⁴ neoarsphenamine is useful in helping to control the course of fever in therapeutic tertian malaria. The results were not

always predictable, and relapses did occur in patients who were given malaria by infected mosquitoes. No effect was obtained, however, with induced quartan malaria, and references to its trial with malignant tertian infections have not been found. Mapharsen has been enthusiastically recommended for the treatment of induced tertian malaria, with a single injection terminating malaria in over 90 per cent of the cases, but eight to ten injections were said to eradicate the malaria permanently. Relapses occurred in only 2 of 24 cases,¹³⁵ but no mention was made of subinoculation of blood in normal persons to determine the radical cure claimed. Young and McLendon¹³⁶ failed to demonstrate curative effects of this drug on induced quartan malaria in Negro parietic patients. Tryparsamide also failed to affect the presence of circulating parasites and viability of blood in 8 patients. In fact, the warning was given that this drug should not be used to terminate induced malaria, because the blood remains infectious, and patients who are discharged may serve as a focus for transmission of the disease. Niven¹³⁷ confirmed the value of Mapharsen for the treatment of induced infections with *P. vivax*, but failed to find any effect against quartan and malignant tertian infections.

Bismuth compounds have been used for the treatment of naturally acquired malaria, but Schwartz¹³⁸ and Cole et al.¹³⁹ have made an important discovery in Thio-Bismol (sodium bismuth thioglycollate) for the clinical control of induced tertian malaria. These workers point out that patients undergoing malaria therapy frequently develop prolonged remittent fever or a double tertian type of infection with a daily paroxysm. The associated symptoms may vary, but physical exhaustion, vascular collapse, persistent vomiting, increasing anemia, rise in icteric index and a rise in the blood urea nitrogen are common. These symptoms need prompt control or treatment with quinine to stop the infection if the patient is to survive.

In the original series of 21 cases of induced tertian malaria receiving Thio-Bismol, the drug was found to possess antipyretic and antimalarial activity. One injection (0.20 gm.) intramuscularly given just before a chill controlled the fever in six to twelve hours and gave a patient an afebrile rest period for two days before the cycle resumed at a typical simple-tertian or forty-eight-hour interval. The untoward symptoms disappeared rapidly during the rest period, and the patient recovered sufficiently to withstand the resumption of paroxysms for their therapeutic effects. Repeated daily injections can be given if a longer rest period is desired, three such injections terminating paroxysms varying from five to thirty-nine days. Pa-

tients treated with Thio-Bismol to control the effects of induced malaria numbered 263, with a mortality of 2.2 per cent. This percentage is compared to the figures of Krauss,¹⁴⁰ in which there was an average mortality of 5.38 per cent among 8354 cases, and of Fong,¹⁴¹ in which there was a mortality of 3.35 per cent among 1012 patients. Consequently, the use of this drug in controlling therapeutic benign tertian malaria provides a significant and decidedly helpful advance.

No satisfactory explanation of the mode of action of Thio-Bismol has as yet been forthcoming. The evidence presented by Cole and his co-workers¹³⁹ substantiates their claim that the drug has antimalarial and antipyretic properties, but the antimalarial action appears to act only against a certain stage of the parasite. If the injection is given to a patient with simple tertian infection more than ten hours before the next expected chill, no effect is observed. The evidence that the drug is assimilated and excreted within twenty-four hours indicates that the therapeutic level in the blood stream is perhaps no longer existent at the time the parasites mature and begin their next asexual cycle. Yet the two-day rest period after injection of Thio-Bismol in remittent and double tertian infections indicates that the drug affects the half-grown parasites in the blood at the time of the injection immediately prior to the chill.

In a recent paper by Young et al.,¹⁴² an effort has been made to determine the effect of Thio-Bismol on various asexual stages of *P. vivax* and also to test the effect of the drug on *P. malariae* and *P. falciparum*. When 0.1 or 0.2 gm. of the drug was injected intramuscularly sixteen to twenty-eight hours after the last paroxysm caused by tertian parasites, future paroxysms by that brood were inhibited. Injections at other hours failed to have any effect. The half-grown parasites decreased in number and in stained films they appeared shrunken, fragmentary, irregularly stained and even free in the plasma of the blood. Yet, according to the opinion of the authors, this degeneration could not alone account for the sharp drop in the number of parasites. The experiments with induced quartan, and malignant tertian infections failed to demonstrate any clearcut action against *P. malariae*, and *P. falciparum* showed the least response of all to Thio-Bismol.

Another interesting and valuable observation by these same authors, was the prompt therapeutic response obtained when Thio-Bismol was injected on the day that the administration of quinine was begun to terminate a tertian infection. The Thio-Bismol inhibited the next paroxysm and the quinine controlled the infection, thus a quicker therapeutic response was obtained than when quinine was used alone.

In passing it should be noted that, here again, a drug has proved to be effective against stages of one species of malaria parasite and not against others. Thus the evidence continues to indicate the individuality of the plasmodia pathogenic for man and the need for pointing research studies toward a solution of the physiologic and biochemical differences that exist between species.

MALARIA IN RETURNING TROOPS

Finally, the following question, frequently asked during recent months, deserves brief consideration: Are troops returning to this country from endemic malarious areas a serious threat to the public health? Even now, frequent references are being made to relapses of malaria in men who have returned from the fighting fronts in the Southwest Pacific and Africa.

An analysis of the serious potentialities reveals that the following factors will play a role in the spread of tropical diseases, including malaria, from returning troops: the time of year when troops return; the presence in the area of necessary vectors for transmission of disease; the type of sanitation in rural or urban communities to which men return; and the occupation taken up by the returned soldier or sailor. The first three factors are the most important ones. If a person harboring malarial parasites in his blood returns during the breeding season of transmitting anopheline mosquitoes, transmission can take place. However, if no anophelines are breeding or can gain access to the infected person, no transmission can occur. With regard to the presence of transmitting vectors during the summer, anophelines that can transmit malaria occur in many of our northern states, including Massachusetts, the only reason for the disappearance of malaria being the absence of human infection. Small epidemics have occurred in scattered northern states in recent years, and future outbreaks may be expected. The explanation of the third factor—sanitation—is obvious. Communities containing numerous breeding places for anophelines, with inadequate screening of houses, a low economic status and poor medical care and supervision are likely areas for the transmission of malaria. Such areas provide the greatest chance for tropical and virulent strains of malaria to gain a foothold.

The experience in England during and after World War I indicates that malignant tertian malaria dies out after approximately one year at that latitude, leaving only endemic benign tertian malaria. In Macedonia, malignant tertian malaria was the most prevalent type among the troops. When these troops returned to England and relapses developed, — approximately 14,000 in 1919,¹⁴³ — the anophelines apparently failed to transmit the infection, because the temperature and hu-

midity requirements for the completion of the developmental cycle did not obtain. Reasons for this failure are well known to malariologists, for malignant tertian malaria is seldom found in regions having an average summer temperature lower than 21°C. (70°F.) and an average winter temperature lower than 9°C. (48°F.). If the infection is brought into such areas, small epidemics may occur, but eventually the disease dies out. Consequently, the major problem with returning troops is to recognize and make an accurate and speedy diagnosis of malaria in all infected persons. Since it is desired to prevent the transmission of new malarial strains in this country, and since there is no need for these men to acquire immunity, a radical cure should be the aim of every practitioner treating such infections.

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NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-SECOND
ANNIVERSARY

House of Delegates, May 10 and 11, 1943

THE House of Delegates convened at the Hotel Carpenter, Manchester, on May 10, 1943, at 7:30 p.m., with Speaker Charles H. Parsons, of Concord, presiding.

The following members answered the roll call.

The President, *ex-officio*
The Vice-President, *ex-officio*
The Secretary-Treasurer, *ex-officio*
Park R. Hoyt, Laconia
Raymond J. Turley, Meredith
W. J. Paul Dye, Wolfeboro
Francis J. C. Dube, Center Ossipee
Walter F. Taylor, Keene
A. C. Johnston, Keene (appointed as alternate for Norris H. Robertson)
Leander P. Beaudoin, Berlin
Arthur B. Sharples, Groveton
Arthur W. Burnham, Lebanon
Leslie K. Sycamore, Hanover
David W. Parker, Manchester (appointed as alternate for George V. Fiske)
Deering G. Smith, Nashua
George C. Wilkins, Manchester (appointed as alternate for Charles H. Cutler)
George F. Dwinell, Manchester (appointed as alternate for Clarence E. Dunbar)
Luther A. March, Nashua
Edward V. Putnam, Warner
Robert M. Lake, Concord
Frederick S. Gray, Portsmouth
Anthony E. Peters, Portsmouth
Edwin D. Lee, Exeter
Roland J. Bennett, Dover
George G. McGregor, Durham
Emery M. Fitch, Claremont (appointed as alternate for Henry C. Sanders, Jr.)
B. Read Lewin, Claremont

The Speaker declared a quorum present, and appointed the Credentials Committee as follows: Drs. McGregor (chairman), Lake and Lee. Dr. McGregor reported that the credentials were in order.

The Speaker appointed the Committee on Officers' Reports as follows: Drs. Peters (chairman), Smith and Sanders. He appointed the Committee on Communications and Memorials as follows: Drs. Putnam (chairman), Campbell and Taylor.

Upon motion duly made and seconded, it was voted to omit the reading of the previous minutes, because of the publishing of the proceedings.

The secretary-treasurer, Dr. Carleton R. Metcalf, presented his report.

MEMBERSHIP, DECEMBER 31, 1942

PAID	
Belknap County	31
Carroll County	13
Cheshire County	30
Coos County	32
Grafton County	68
Hillsborough County	128
Merrimack County	65
Rockingham County	59
Strafford County	34
Sullivan County	18
Not in county society	4
	<hr/> 462
UNPAID	
Affiliate members	24
Honorary members	6
Members in the Service	39
	<hr/> 69
Total	<hr/> 551

The total membership on December 31, 1941, was 543

FINANCIAL STATEMENT

RECEIPTS	
January 5, 1942—Balance forward	\$97 66
Belknap County	192 00
Carroll County	72 00
Cheshire County	180 00
Coos County	192 00
Grafton County	378 00
Hillsborough County	776 00
Merrimack County	390 00
Rockingham County	318 00
Strafford County	204 00
Sullivan County	102 00
<i>New England Journal of Medicine</i> subscriptions	9 00
Net receipts, 1942 annual meeting	252 65
Cash received at annual meeting	98 00
Receipts from members not in county societies	24 00
Receipts from trustees from general fund	1100 00
Refund, Cancer Commission	5 65
Women's Auxiliaries	130 00
Donations to National Physicians' Committee	205 00
	<hr/> \$4755 96

EXPENDITURES	
<i>New England Journal of Medicine</i>	\$447 04
Journals	9 00
Full subscriptions	8 40
Tables	5 00 92
Transactions	—

Concord Photo engraving Co. (half-tone cuts) . . .	25.60
Carleton R. Metcalf (salary)	400.00
Bridge and Byron (printing)	119.32
Envelopes and stamps	58.42
Frank J. Sulloway (retaining fee)	100.00
Robert O. Blood (telegrams and telephone calls) . . .	20.82
Robert O. Blood (clerical work)	150.00
Women's Auxiliary	100.00
Benevolence Fund	609.00
The Barwood Press (Committee on Education and Hospitals)	5.00
Florence McCann (Committee on Education and Hospitals)	20.18
Robert H. Morris (expenses at jurisprudence meeting)	25.00
American Medical Association (pamphlets)	6.00
American Medical Association (<i>American Medical Directory</i>)	15.00
Edward Blank (cancellation of <i>New England Journal of Medicine</i> subscription)	3.00
W. H. Butterfield (refund to men in Service) . . .	18.00
W. H. Butterfield (dues collected at annual meeting)	14.00
Leander P. Beaudoin (dues collected at annual meeting)	21.00
Deering G. Smith (medical preparedness expenses) . . .	276.61
Deering G. Smith (dues collected at annual meeting)	70.00
Deering G. Smith (expenses at American Medical Association meeting)	86.30
Frederick S. Gray (dues collected at annual meeting)	7.00
George C. Wilkins (Cancer Committee)	50.00
Madeline A. May (stenographer at 1941 annual meeting)	255.00
Madeline A. May (stenographer at 1942 annual meeting)	278.08
C. R. Metcalf (lunches for out-of-state guests at annual meeting)	7.00
Richard Schatzki (expenses at annual meeting) . . .	2.60
R. W. Tuttle (expenses at annual meeting)	65.00
W. H. Barker (expenses at annual meeting)	48.74
Paul D. White (expenses at annual meeting)	4.62
Fred Adair (expenses at annual meeting)	117.00
Beatrice M. Kesten (expenses at annual meeting) . . .	24.60
The Robbins Company (gold medal)	33.30
National Physicians' Committee (Grafton County) . . .	75.00
National Physicians' Committee (Belknap County) . . .	30.00
National Physicians' Committee (Hillsborough County)	100.00
National State Capitol Bank (service charges during year)	4.29

\$4510.84

Balance January 1, 1943 248.12

\$4758.96

Refund to *New England Journal of Medicine*
(cancellation of Dr. Blank's subscription) . . . 3.00

\$4755.96

CARLETON R. METCALF, *Secretary-Treasurer*

Dr. Lord, a trustee, made a statement of fact regarding finances, as follows:

Dr. Metcalf has said that our funds are going downhill pretty fast. I think you know that the Society has

something over \$20,000 in different funds, and most of the funds are earmarked for special purposes, such as the Pray Fund and the Benevolence Fund. But there is the fund that we call the General Fund, totaling about \$10,000, from which we can draw in emergencies. I should like to tell you a little of what has happened to the Fund.

On May 1, 1940, the date on which the Trustees' report is made up, the General Fund had on hand approximately \$11,800. On May 1, 1941, it had on hand approximately \$10,897. The next year,—this will have to be stated as of January, 1942, because we have changed our period, so that it is less than a year,—the Fund had on hand approximately \$10,000, which is \$800 less than the year before. In January, 1943, it had on hand approximately \$9192, a further decrease of \$800. From January, 1943, to May 10, 1943, it lost about \$300 more. Thus the Fund is continually going downhill. The total has diminished in a little over three years (from May 1, 1940, to May 10, 1943) from \$11,800 to \$8000, or about \$3000.

The reason for this diminution is as follows: Ordinarily, the General Fund is not used for the expenses of the Society, because those expenses are handled from our ordinary income, but when an emergency arises, the Society can vote to spend certain sums. The first year, \$1000 was put into the General Fund itself to raise the total. The next year, 1941, we spent \$1000 and thereby increased the Benevolence Fund. In 1942, we spent \$1000 for the sesquicentennial celebration. During the past year, for the reasons that Dr. Metcalf gave you, we spent \$1100 extra, and since January 1, 1943, we have added another \$356, which is for the Procurement and Assignment Service. By that means, our total has been reduced to \$3000.

The income of the General Fund last year was \$223. Now, if our expenses for next year are something like \$1000 or \$1100, such as we paid this year for general expenses, plus the Procurement and Assignment Service,—if the latter costs what it did this year,—the total expenses will be about \$7450. The income being a little over \$200, we shall have a net loss of about \$1250 during the coming year, if the war keeps on.

I understand also that we have 551 members. The number of men in the Service is, I believe, 114. This leaves about 440 men who are paying dues for 551 members. If the net loss for the coming year is \$1250, we shall have to pay \$3 per man to make up for it. Do you want to keep the fund up to an approximate \$10,000? If you do, you will have to do something to bolster it up.

Secretary Metcalf replied as follows:

We hope to economize to the following extent this year: The Procurement and Assignment Service, according to Dr. Deering Smith, will be much less expensive this year than it has been in the past. Also, we are having a one-day meeting, which is less expensive than a two-day meeting. We have chosen all our speakers from New England, so that we are saving on the traveling expenses of men from outside cities like Chicago, Rochester, Minnesota, Philadelphia and New York. The Auxiliary has ordinarily received \$100 toward its meeting, but this year it is not receiving anything. My only other suggestion is the one

that I made in my address which is the elimination of the *New England Journal of Medicine*. This would mean a saving of about \$600 a year, but in the past this step has been considered penny wise and pound foolish.

Dr Johnston suggested that the dues be raised by the amount specified by Dr Lord, to keep the organization going as before.

Dr Burnham asked what was the use of having a large General Fund if it was not to be spent in such times as these. He saw no occasion for alarm. He thought that it was permissible to raise the dues if necessary, but why was it essential to have \$10,000 in the General Fund? Even if the Society was now spending more than usual, and the Fund was going down, he saw nothing to worry about unless it should drop to about \$1000, in which event it could be built up. The situation would probably adjust itself after a fashion. The commonsense thing to do was to let the Fund stay as it was unless it fell to a low level, when the members could be assessed \$2 or \$3 extra to bring the Fund up again.

The Speaker then appointed the Committee on Nominations as follows: Drs Dye (chairman), Burnham, Wilkins, Fitch and Beaudoin.

The Committee on Officers' Reports commended the faithful and efficient work of the Secretary, Treasurer, and the chairman, Dr Peters, moved the adoption of that portion of the report. This motion was duly seconded and was carried.

Dr Peters then spoke as follows:

The committee recognizes the continuing decrease in revenue of the Society, due to the war, which is being partially offset by the economies effected by this one-day meeting. It is recommended that the *New England Journal of Medicine* be continued to be sent to all members, including those who are in the Service.

Serious consideration as to the raising of the dues must be given, because it does not seem wise to draw on the General Fund too heavily to make up our deficit.

Dr Peters moved the adoption of this part of the report, and the motion, duly seconded, was carried.

Dr Peters then added that the committee recommended that the Committee on Nominations this year exclude members in the Service, although they will be properly carried on the membership lists. He moved the adoption of this part of the report, and the motion, duly seconded, was carried.

Reports of Councilors

BELKNAP COUNTY

The Belknap County Medical Society held six meetings from November to April, inclusive. The meetings were

all held at the Laconia Tavern. Dinners were served and were followed by programs. The meetings were well attended, the men from the north coming when it must have been a great effort.

The society has 7 men in the armed services. This in a small society is very noticeable, throwing a decided burden on those in active practice.

The society has 37 members.

C S ALFORD

CARROLL COUNTY

We have a very small group with infrequent meetings of the county society as a whole but fairly frequent usually monthly, assemblies of the several hospital staffs.

The present report largely consists of an account of the annual meeting of the society held on April 14, 1943 at Huggins Hospital, Wolfeboro. The exigencies of the war, as expressed by restrictions in travel and more work for the fewer physicians left at home, have prevented more meetings of our society this year. It was unanimously voted that the secretary remit \$1 per capita of the membership of the society to the National Physicians Committee as a contribution and as an expression of approval of the fine work it has done.

A motion that the society go on record as approving the Medical Insurance and Enabling Act now under consideration by the New Hampshire State Legislature was unanimously carried.

The following officers for the ensuing year were unanimously elected: Drs F J C Dube and W J P Dye delegates to the annual meeting of the New Hampshire Medical Society; Dr Dube, president; Dr Ralph W Tuttle, vice president; and Dr Charles E Smith, secretary treasurer.

A talk was given by Dr Dye covering the war sessions meeting of the American College of Surgeons held in Boston on March 15, 1943. Various medical facts concerning military and naval medicine that had brought forth new procedures because of wartime problems were discussed.

A thorough discussion of the value of the Stader skeletal traction, reduction and immobilizing splint in which the patients have free motion of the joints above and below the fracture and are largely ambulatory, was presented through reports of the Navy medical officers who participated in the Boston meeting. It appears that this may be a great advance in the treatment of fractures provided the excellent results shown in the large number of cases now treated and under observation by the Navy Medical Corps continue to be obtained.

The wartime trends of medical education, whereby all medical students will be enlisted in a branch of the armed forces with their tuition paid by the Government were brought out. Further mention was made of the help that nurses, aides and other voluntary organizations are giving to depleted hospital personnel.

It was stressed that Civilian Defense has accomplished a great deal in the organization of communities for disasters, as aptly proved by the excellent management of the Coconut Grove fire and it was hoped that practice interest and study would be continued along these lines.

At the same meeting Dr Frank H. Lahy, chairman of the Directing Board of the Procurement and Assignment Service, gave some interesting and instructive remarks concerning the operations of this committee. He stated that Massachusetts, Connecticut and New York

which are largely metropolitan and urban districts, were considerably behind in their quotas of physicians for the armed services. It was noted that the medical profession had been given the privilege of classifying its own members as available or essential, and to date the majority of men so classified as available, except in the three states above mentioned, had promptly voluntarily applied for their commissions, so that quotas for last year were met. Dr. Lahey voiced the hope that quotas would be met this year in the same voluntary fashion, so that the members of the medical profession would prove worthy of the privileges conferred upon them, but he warned that if quotas were not met, some compulsory method might be instituted to supply Army and Navy medical officers.

W. J. PAUL DYE

CHESHIRE COUNTY

The Cheshire County Medical Society held two well-attended meetings during the past year.

The spring meeting was held at the Eliot Community Hospital. At this meeting papers were read, and discussions followed each paper. After the meeting, dinner was served by the hospital to all members of the society.

At the second meeting no papers were read but the time was given to discussion of local and state medical questions. Six members of our society have joined the armed forces, 5 from Keene and 1 from Troy.

The secretary reported that all the doctors in the county belong to the society and that all are in good standing.

JOHN J. BROSNAHAN

COOS COUNTY

The officers of the society, after conferring together, decided not to hold a meeting this year, largely owing to difficulties of travel and the unavailability of a speaker.

The society has 6 members serving in the armed forces, and there are 2 nonmembers so engaged.

The former officers are serving the society for another year.

RICHARD E. WILDER

GRAFTON COUNTY

The Grafton County Medical Society has continued its policy of holding two meetings each year.

At the regular business meeting held at Hanover in the fall, 3 new members were elected. It was voted to continue participation in the program for medical care sponsored by the Farm Security Administration. A contribution of \$75 to the National Physicians' Committee was voted.

A discussion on "Virus Pneumonia" was presented by Drs. Sven Gundersen and Colin C. Stewart, Jr., of the Hitchcock Clinic.

The spring meeting will be held at Hanover on April 28, 1943. The program will consist of a discussion on infantile paralysis.

ARTHUR W. BURNHAM

HILLSBOROUGH COUNTY

The Hillsborough County Medical Society has changed its former time of meeting, and has instituted evening meetings following a dinner.

The business meeting was held in the fall at Manchester, New Hampshire, with 75 members present. New officers were elected as follows: Dr. G. Hoffses, president;

and Dr. S. Fraser, vice-president. Dr. Charles Parsons, head of Civilian Defense for New Hampshire, gave a brief outline of the work in this state. President Thibodeau introduced Dr. Dudley Ricker, regional medical officer, who gave a fine talk on preparations being made for civilian defense in this corps area.

The 1943 spring meeting was held at the Nashua Country Club, with Dr. Hoffses presiding. Reports showed that we have 146 members and that 34 of these are in the armed services, which is about 25 per cent of the membership.

The medical program was conducted by the Medical Department of Grenier Field, and was participated in by Lieutenant-Colonel Fresh, Major Hubbard and Lieutenant Reitz, Captain Hardenbrook, Captain Driggs and Lieutenant Hermann. Captain Coughlin, Major Tate, Major Babson and Captain Butterfield also participated. This proved to be a most interesting program, and the society suggests that some other county society put on a similar program.

During the past year we have lost 2 members: Dr. Herbert S. Hutchinson, of Milford, the second oldest member in the society, and Dr. Norman D. Webber, of Manchester.

We have the largest membership in the history of the society, and attendance at our last meeting excelled all others.

C. O. COBURN

MERRIMACK COUNTY

A social meeting was held on July 7, 1942, at the Franklin Country Club, with 25 members present. A demonstration of resuscitation was given. Dr. Chancy Adams acknowledged a gift as a member of fifty years' practice.

At a meeting on October 6, 1942, at the Eagle Hotel, Concord, Major W. W. Babson, M.C., U.S.A., discussed the present-day treatment of burns.

The annual meeting was held on January 5, 1943, at the Eagle Hotel, Concord. It was voted to send a message of sympathy to the family of Dr. A. K. Day. Three new members were admitted to the society. Dr. Metcalf spoke on group hospitalization.

A meeting was held on April 6, 1943, at the Eagle Hotel, Concord. It was voted to hold the summer meeting at New London. Major John S. Wheeler, state medical director of Selective Service, discussed some medical problems in connection with his organization. Mr. Spaulding, New Hampshire director of the Blue Cross, explained the system of hospitalization.

The following members are in the Service: Donald Barton, Lee C. Bird, John H. Branson, Warren H. Butterfield, Eugene Chamberlain, Joseph M. Clough, Carl A. Dahlgren, Raymond P. Galloway, MacLean J. Gill, Thomas J. Halligan, Oliver S. Hayward, Philip M. L. Forsberg, Harold D. Levine, Joseph McCarthy, J. K. McLeod, Herbert B. Messinger, J. Dunbar Shields, Ellsworth M. Tracy, Jules Weinberg and John S. Wheeler.

WARREN H. BUTTERFIELD

ROCKINGHAM COUNTY

The annual meeting of the Rockingham County Medical Society was held on October 28, 1942, at the Portsmouth Hospital. Twenty-six members were present. After the usual business meeting, lunch was served by the hospital.

Two interesting papers were presented one by Dr J F Holmes, Manchester, on Slipping Rib Cartilage, and the other by Lieutenant Commander E Ross Mintz (MC), USNR, on Some Urologic Aspects

The date for our spring meeting has not been selected

CLEON W COLEBY

STRAFFORD COUNTY

For the year 1942 the society had 28 active and 6 affiliate members. Four members are in the United States Army and 1 is serving with Pan American Airways in Africa.

The annual meeting was held on October 28, 1942, at the Lincoln House, Dover. There were 23 members and guests present. Dr H Bristol Nelson of the Boston Lying in Hospital spoke on "Very Dry Problems in Obstetrics."

The spring meeting, to be held on April 28, is now being planned. It is expected that we shall be forced to accept educational films in lieu of a speaker.

In accordance with the action taken last year in the House of Delegates of the New Hampshire Medical Society, \$1 for every active member has been sent to the National Physicians Committee.

There were no deaths among our members during the fiscal year, nor were there applications for membership. There is one request for transfer from York County (Maine) to be acted on at our next meeting.

J A HINTER

SULLIVAN COUNTY

The Sullivan County Medical Society held three meetings during the past year.

The first meeting, held in Claremont, consisted of the election of officers and routine business, including a discussion of the man power problem, in view of doing our part in supplying doctors for the armed forces.

The second meeting, in June, was a joint meeting with the Crawford County Society, addressed by Dr Deering Smith on Procurement and Assignment.

The third meeting in Claremont was a symposium on infectious diseases, led by Dr Edward Pease of Boston. These meetings were all well attended and much interest was shown in keeping the society in touch with the state problems.

EMERY M LITCH

Dr Putnam then made his report as chairman of the Committee on Communications and Memorials. He first presented a communication from the New Hampshire State Department of Public Welfare.

Dear Dr Metcalf

In accordance with an established plan of rotation Dr John A Coyle, of Hanover and Dr Raymond Ingalls of Berlin are retiring as members of the Medical Advisory Committee on Eye Conditions, which assists the Department of Public Welfare in adequately handling medical matters in connection with the state's blind and prevention-of-blindness program.

To replace Dr Coyle and Dr Ingalls the department recommends Dr Hermann Burian, of Hanover, and Dr Edward McGee, of Berlin. Both doctors have accepted our invitation to serve. In order that

the records may be kept up to date and the state medical society may be kept informed on all departmental matters relating to the medical-care field I am writing to request that the House of Delegates approve Dr McGee's and Dr Burian's acceptance of an appointment to this committee.

(Signed) ELMER V ANDREWS
Commissioner

On motion duly made and seconded, it was voted that the House of Delegates approve Dr McGee's and Dr Burian's acceptance of their appointment to the Medical Advisory Committee on Eye Conditions.

Dr Putnam then presented a letter from the New Hampshire Hospitalization Service.

89 North Main Street, Concord
January 17 1943

Dear Dr Metcalf

It is the desire of the New Hampshire Hospitalization Service to secure the full approval of the New Hampshire Medical Society for its activities in the State.

As you know, the Blue Cross is established as a nonprofit corporation, is operated as a public service and has met all the requirements of the American Hospital Association and has received the approval of that organization. It has been approved by the New Hampshire Hospital Association.

We would also like your permission to inform the public of your approval.

If there are details of our corporate structure or purpose on which you desire information, I would be very glad to provide it.

(Signed) R S SPALDING
Executive Director

Dr Putnam recommended the approval of the hospitalization plan and the motion, duly seconded, was carried.

Dr Putnam then presented a letter from the National Conference on Medical Service. He said that the main purpose of the letter seemed to be the seeking of approval of a resolution that would authorize a Committee on Medical Service of the American Medical Association, which would have some sort of liaison office in Washington for the purpose of improving medical service care. The letter was accompanied by the following resolution.

WHEREAS, Social and economic changes have altered the lives of our citizens, and the federal government has found it necessary to issue directives from time to time, we as physicians believe that it is our duty to take a more active part in the creation of such regulations as affect the practice of medicine, therefore, be it

RESOLVED That this National Conference on Medical Service go on record as favoring the immediate

development of a stronger national economic and legislative policy governing the practice of medicine and that such a policy be integrated with each state and county, and be it further

RESOLVED, That the expression of this National Conference on Medical Service be submitted to the Board of Trustees of the American Medical Association, advising them that this resolution, or a similar one, will be submitted to the delegates of the American Medical Association at their next annual meeting.

Dr. Putnam said that the Committee on Communications and Memorials had no recommendations on this particular letter. On questioning by the speaker, Dr. D. G. Smith replied that he had nothing to say regarding the communication. Dr. Putnam added that, included with their letter was a resolution that they proposed to the House of Delegates of the American Medical Association, to be submitted to that body at the annual meeting. (Dr. Putnam then read the letter.)

In answer to a question, Dr. Putnam stated that approval of this resolution was sought. It was to be forwarded to the National Conference of Medical Service, and the resolution would then be presented to the House of Delegates of the American Medical Association at its annual meeting.

Dr. Dwinell expressed the opinion that the American Medical Association was opposed to the presence of any legislative or lobbying organization in Washington. He believed that the purpose of the National Conference on Medical Service was to place in Washington some such group that was not connected with the American Medical Association.

The speaker requested Dr. Putnam to talk the matter over with Dr. D. G. Smith and make a report in the morning.

Dr. Putnam, speaking in behalf of the Committee on Communications and Memorials, then recommended that the House of Delegates of the Society be put on record as favoring the basic principle of having a liaison representative in Washington. This he thought should be done either through existing committees or in a manner deemed best by the American Medical Association.

Upon motion duly made and seconded, the report of the Committee on Communications and Memorials was accepted.

Dr. Woodman then made his report as chairman of the Committee on Amendments to the Constitution and By-Laws, as follows:

Last year, there were two changes in the by-laws which would change the wording in two sections. One was that Chapter VIII, Section 10, be amended to read as follows:

The Committee on Mental Hygiene shall consist of three members, whose duties shall be to study this special subject, co-operate as far as possible with the heads of the state institutions under medical supervision, and report to the Society.

This leaves out the word "Social" and makes it strictly a committee on mental hygiene.

Then, there was another change; it was recommended that the Committee on Medical Education and Hospitals should consist of three members. This change was in Section 12.

Those were changes in the by-laws, and they were consummated by being permitted to lie over one day.

A change in the constitution proposed by Dr. Smith is to the effect that Article XII be deleted. Article XII reads as follows:

Article XII. *New England Medical Council.* This Society shall be privileged through its House of Delegates to join with other New England state medical societies, and to participate in the activities of the New England Medical Council.

The New Hampshire Medical Society shall be represented in this body by the President, Secretary, Treasurer and three delegates-at-large. The three delegates-at-large shall be appointed by the President, one for one year, one for two years, one for three years; annually thereafter he shall appoint one for three years.

This, apparently, should be acted on at this meeting.

A change suggested by Dr. Wilkins is that Article XIII of the constitution be made Article XII. This should also be acted on at this meeting.

On the recommendation of Dr. Peters of the Committee on Officers' Reports, it was voted that the report of the Committee on Amendments to the Constitution and By-Laws be accepted as read.

On motion of Dr. Wilkins, the changes in the constitution as presented by Dr. Woodman were adopted.

A verbal report of the Committee on Child Health by Dr. Colin C. Stewart, who was unable to file a written report, was accepted on the recommendation of the Committee on Officers' Reports.

The report of the Committee on the Control of Cancer was presented by the chairman, Dr. Wilkins.

Report of the Committee on the Control of Cancer

Three short letters giving information on three pertinent aspects of cancer control were sent to every physician in New Hampshire. Of the three letters, perhaps the most important for reference filing was a concise but comprehensive discussion of biopsy methods, instruction in taking biopsies, where to take them from and how they should be prepared if mailed to a laboratory. The importance of a brief but good history, with the patient's name, age and a description of the tumor, was noted. Another letter described proper methods of examining and taking biopsies from women with abnormal flowing. The purpose of this letter was to explain not

only how to determine the cause of bleeding but to state emphatically that no patient should be treated with x-ray therapy for abnormal bleeding without preliminary examination of the cervix, if no disease was discovered there, the uterus should be curetted under general anesthesia and a pathological report should be awaited before proceeding with any treatment. Too many cases have been observed where cancer of the cervix or fundus has not been discovered until too late for successful treatment, both the patient and the doctor having been lulled into a feeling of false security because irradiation temporarily stopped flowing. The third letter discussed carcinoma of the vulva and stressed particularly the necessity of a radical vulvectomy in all cases, with later node dissection on the affected side. It was explained that incomplete operation almost invariably is followed by recurrence.

We hope these letters may be useful in bringing some thing new or something that has been forgotten, to the attention of the busy physician or surgeon. The subjects that have been discussed in all our letters since 1934 have been on phases of cancer diagnosis or treatment that, from observations made in clinics and laboratories have shown the need for further education of the physician.

The fourteen diagnostic clinics and treatment centers have continued their excellent work. Twelve years ago there were one cancer clinic, one supply of radium and three deep therapy x-ray machines in the state. Today there are fourteen clinics, of which seven are treatment centers. There are 800 mg of radium available and there are ten deep-therapy machines. New Hampshire has more cancer clinics per population than any other state and eleven of the fourteen clinics have been approved by the American College of Surgeons. Transportation difficulties have reduced the number of patients coming to the clinic, not so much among those with cancer, but it has reduced the number of those not actually having cancer, and unfortunately it is difficult for patients who have been treated to return regularly for check ups. Last year 54 per cent of the new patients examined in the clinics had cancer compared with 36 per cent in 1934.

The Women's Field Army continues its important and notable work in carrying out its educational program among the laity, through the distribution of thousands of pamphlets, arranging cancer talks before groups, radio broadcasts and moving pictures before groups and in schools. Many physicians have given talks before groups and on the radio. The Women's Field Army also assumes the expenses of transportation of many indigent patients to and from clinics and hospitals. Another activity is making surgical dressings for indigent cancer patients. These dressings are made from old cotton and linen combined with cellulocotton.

The Executive Committee of the Women's Field Army will soon consider the advisability of establishing a fund from which amounts may be drawn to cover the expenses incident to a three or four weeks training course in cancer diagnosis and treatment. It is suggested that this be offered to physicians associated with our cancer clinics and selected by the hospital staffs. It is believed that the use of this money to carry on further education of physicians interested in cancer and its treatment would be an admirable way to return to the citizens of the state some of the investments made in the work of the Women's Field Army. This will require acceptance of the plan by the hospitals, the American Society for the Control of

Cancer and certain teaching hospitals with large cancer services.

The Women's Field Army constantly urges periodic physical examinations as one way of discovering cancer early, and the medical profession can aid this recommendation by hearty approval of the principle and by giving a really thorough and comprehensive examination when requested.

Your committee spent \$40.80 for printing stationery and postage. The balance of our \$50 appropriation has been returned to the treasurer. We request an appropriation of \$50 for the coming year.

GEORGE C. WILKINS, *Chairman*

RALPH E. MILLER

GEORGE F. DWINELL, *Secretary*

Dr. Peters, speaking for the Committee on Officers' Reports, recommended that the Committee on the Control of Cancer encourage the proposal that physicians associated with cancer clinics be assisted in the manner contemplated by the Executive Committee of the Women's Field Army, which would cover expenses for a three to four weeks' training in cancer diagnosis and treatment. The motion was carried.

The Committee on Officers' Reports further recommended that the request for an appropriation of \$50 for the ensuing year be approved. The motion was also carried.

The report of the Committee on Medical Economics was made by Dr. Leslie K. Sycamore.

Report of the Committee on Medical Economics

National Physicians Committee. The work of the National Physicians' Committee for the Extension of Medical Service is of continuing importance and your committee makes the same recommendation as last year that a contribution of \$1 per capita be made by each county society, to be transmitted to the National Physicians Committee through the treasurer of the New Hampshire Medical Society.

Prepayment Medical Service. As directed by the House of Delegates at its last session, an enabling act was introduced into the present session of the Legislature and has been passed by both houses. This act permits the establishment, under regulation of the State Commissioner of Insurance, of a medical service corporation for furnishing medical care on a prepayment insurance basis. Your committee has continued its study of such plans as are now in existence and recommends that a definite plan be drawn up for the establishment of a medical service corporation in New Hampshire, such plan to be submitted to the next meeting of the House of Delegates for its approval.

Medical Care Program for Farm Security Clients. This program continues to function satisfactorily in Grafton and Cheshire counties with 100 per cent payment of bill for physicians' services during 1942.

LESLIE K. SYCAMORE

FRANCIS J. C. DUBE

Dr. Peters for the Committee on Officers' Reports moved the adoption of that portion of the report relating to the work of the National Physicians'

Committee. The motion, duly seconded, was carried.

Dr. Peters said that in view of the fact that the enabling act has since become a law, it was recommended by the Committee on Officers' Reports that a definite plan be drawn up by the Committee on Medical Economics and Mr. Sullo-way for the establishment of a medical-service corporation in New Hampshire and that such plan be submitted to the next session of the House of Delegates for its approval. He moved the adoption of this portion of the report.

Dr. Metcalf then spoke as follows:

This enabling act, which has been signed by the Governor, permits any corporation to work out this particular problem of prepayment of all medical care on the insurance basis under the supervision of the Commissioner of Insurance. The Blue Cross, which has a hospitalization plan, is interested in this. I do not know, if they undertake it, when they will want to do so. It is perfectly possible that they might like to get going before the first of the year, or before the expiration of another year.

If any corporation wishes to undertake this plan, it may be desirable to get in touch with it and have a perfectly definite plan worked out before the next meeting of the Society. In other words, it is going to delay the whole thing a year if we turn it over to the Committee on Medical Economics and have them report a year from now, and then work out something with some corporation. If any plan is adopted, of course, it must be one that will appeal to the doctors, and that will have a sufficiently low premium rate so that it will appeal to the public, and there are many details with which the insurance companies are familiar that must be incorporated and must be studied. Shall these patients be patients in hospitals? Shall such a plan provide for house visits and office visits? Shall it provide for x-ray work? All these details have to be worked out.

The thing has to be on a basis which can be sold to the public in groups and which will also ensure a fee that is adequate for the doctor, and that will not be any cut-rate proposition.

I do not know the best way to go about it. There is a question in my mind whether the thing ought not to be expedited as much as it can be, if the plan is going to come to fruition.

Dr. Wilkins thought that the simplest procedure would be to work with the Blue Cross representatives who were handling the hospitalization problem in New Hampshire. He said that in Massachusetts, the Blue Shield was being conducted through the office of the Blue Cross, and that since prepayment hospital insurance was already in operation in the State, he was inclined to think that probably it would work out better if co-operation could be obtained with that group to carry on this work.

Dr. Sycamore said that it was the opinion of the Committee on Medical Economics that to draw up such a program would require considerable time and that it could be expedited if necessary. It was felt that it was an important enough program, so far as the medical profession was concerned, to be brought before the House of Delegates and approved before any such plan could be put forth. If the House of Delegates thought that such a program should be expedited, a special meeting of the House could be called for that purpose. It was a part of the provision of the enabling act that the Trustees must be approved by the New Hampshire Medical Society, and this would have to be done before any such plan could be started. It had been the experience in places where such plans were functioning that the simplest way to handle them was through the Blue Cross, if that organization was working in the state in which the plan was introduced. Such a procedure could probably be worked out in New Hampshire.

Secretary Metcalf said that after talking with Mr. Spaulding, the Blue Cross representative, he had decided that any committee—the Committee on Medical Economics, if it drew up the plan—ought to go over the situation with the insurance people, because Mr. Spaulding had pointed out to him various things from an insurance standpoint that had not occurred to him. The plan might have to be worked out through the county societies rather than through the State Society, because the bill specified that 50 per cent of the men in a given area must sign up for the plan if it was to be put into effect in that area. He did not know what an area was, but supposed that a logical one would be a county. He suggested that the Committee on Medical Economics might go over the whole thing with the Blue Cross and draw up some scheme that they thought was workable and that the committee thought would appeal to the doctors. They could determine what an area was and so forth, so that when the plan was reported to the Society a year later, it would be a full-fledged one that would stand up under criticism.

Dr. Sycamore replied that that was the intention of the recommendation.

Dr. Peters asked when the plan must be reported, and whether it was proposed to hold a special session. Secretary Metcalf thought that this question would rest with the Committee on Medical Economics. A special session would be difficult to organize.

Dr. D.-G. Smith proposed that a copy of the plan be submitted to the House of Delegates in

advance of the next session so that it would have an opportunity to go over it.

Dr. Wilkins pointed out that this would cause too much delay, and proposed that the committee study the proposal and make a report on it. They might be able to make a report in six months and send a printed report to the House of Delegates, and possibly get some action. This would be preferable to delaying the matter, for a whole year.

President Rock suggested that the Committee on Medical Economics and the officers of the Society take the matter up and make an early report.

Dr. Peters felt sure that if such an amendment was made, the Committee on Officers' Reports would concur.

Secretary Metcalf asked whether the time element could be omitted, and the committee and officers asked to report either at a special session or at the next regular session.

Dr. Wilkins thought that this would be acceptable.

Speaker Parsons asked Dr. Smith to withdraw his motion, with Dr. Dye's permission, and restate it with this qualification.

Dr. Smith agreed that the next session might be a regular session or a special session.

Dr. Wilkins said that he believed the President's suggestion should be embodied and that the

Committee and the Officers of the Society should work on this proposition.

Dr. Peters presented a new recommendation, namely, that a definite plan be drawn up by the Committee on Medical Economics, with the officers of the Society, for the establishment of a medical-service corporation in New Hampshire, such a plan to be reported as early as possible.

A member asked whether the plan would have to be ratified by the Society as a whole or simply by the Delegates. Speaker Parsons replied that ratification would be by the Delegates only, since they are the governing body.

Dr. Fitch agreed with the Secretary that a special session was difficult to manage, and asked whether, if the matter could be expedited so that it could be handled by the committee and the officers, as adequate an opinion could be obtained from the Society as would be done by calling a special session.

Dr. Dye asked whether it was possible to decide by a nonassembled vote. Dr. Smith then moved that the plan after being proposed by the committee be submitted to the members of the House of Delegates for their approval or disapproval, by a nonassembled vote, and that the House of Delegates authorize the action of the members in this nonassembled group in advance. The motion, duly seconded, was carried.

(To be concluded)

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 29331

PRESENTATION OF CASE

A seventy-five-year-old physician entered the hospital because of a painless mass in the upper abdomen.

He had been in excellent health until eight years prior to admission, at which time, while riding in the back seat of a car, he received a heavy jostling in going over a bump; he felt as if something had been torn loose in his upper abdomen. Three years before entry he noted a firm mass in the epigastrium. Two years before entry he overworked during the remodeling of his house and had an attack of midepigastria pain, which radiated toward both flanks. This was followed by several attacks of faintness and sweating, one of which occurred after a home obstetric case in which the delivery was performed on a low bed, and was associated with some vertigo and ringing and pulsating in the ears without deafness. He was seen by a physician, who advised rest. This he did for two weeks but then resumed his normal busy life. He was free of pain until fourteen months before admission, when he again strained himself while working about his car. He had epigastric pain radiating to the right and left. This time the pain was much severer. It gradually subsided, however, after he had rested for a week. In the interim the abdominal tumor had steadily increased in size so that when he sat in certain positions he had an annoying sensation. There was no history of disturbances of appetite or bowel movements. No weight loss was noted.

He had had typhoid fever at the age of twenty-five.

Physical examination showed a tall, large-boned man in no discomfort. Hyperkeratotic lesions were present over the dorsum of both hands. The lungs were hyperresonant. The cardiac borders could not be determined because of emphysema. The heart sounds were normal in volume, rate and rhythm. There was a blowing systolic murmur, best heard in the aortic area. The second sound was snapping. The upper abdomen was protuberant. A large, firm, irregular, movable mass

about 15 cm. in diameter was palpable in the upper midabdomen. It was nontender and the abdominal wall was movable over it. It transmitted strong aortic pulsations.

The blood pressure was 170 systolic, 100 diastolic. The pulse was 80 and of large volume. The temperature and respirations were normal.

On the evening of admission, about three hours after having been examined, the patient asked for an ampule of Coramine. He was found to be perspiring profusely. His skin was pallid, cold and wet. He was extremely weak and felt faint. He had a desire to move his bowels and passed a small semisolid fecal mass, which was guaiac negative. The pulse was 64, the blood pressure 100 systolic, 70 diastolic. One-sixth grain of morphine was administered. The patient remained pallid throughout the night. Early the next morning the blood pressure was 66 systolic, 30 diastolic, and the pulse below 70. His condition steadily improved in the next twelve hours.

An electrocardiogram on the day following admission showed a normal rhythm. The rate was 70. The PR interval was 0.2 second. The T waves were upright in Leads 1 and 2 and low in Lead 3. There was slight sagging of the ST segment in Leads 1 and 2. There was some evidence of left-axis deviation. In the chest leads, the QRS waves were normal and the T waves showed slight late inversion in CF₂ and were upright in CF₄ and CF₅.

The white-cell count was 6500, with 72 per cent neutrophils; the hemoglobin was 9.8 gm. There was moderate achromia, as well as variation in size and shape of the red blood cells; the platelets were diminished. The blood nonprotein nitrogen was 42 mg. per 100 cc. The urine was normal.

X-ray examination of the abdomen showed a large homogeneous soft-tissue mass extending from the epigastrium to the iliac crests, apparently displacing the transverse colon downward. The hepatic and splenic shadows were not identifiable. The left kidney shadow was clear; the right could not be visualized.

The patient was transfused with 500 cc. of blood, and an abdominal exploration was performed on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. ARTHUR W. ALLEN: I just asked Dr. C. Sidney Burwell what he thought about the electrocardiographic findings and he said that they were not very exciting. That is as far as he would go. Surgeons are not supposed to know how to interpret these readings. We have the interpretation made for us by the internists, so I shall accept Dr. Burwell's opinion.

*On leave of absence

May we see the x-ray films?

DR. MILFORD SCHULZ: This shadow represents the very large, upper abdominal mass. You can see the psoas contours through it, so that I suspect it does not arise in the retroperitoneal area. The kidneys are visible and not enlarged. I believe that this shadow up here is the spleen. If it is, it is not enlarged. The lateral film is somewhat thin and shows the mass to extend almost to the anterior abdominal wall. There are no areas of calcification. When one holds the film obliquely one can just make out the spine, in which there appears to be no erosion.

DR. ALLEN: We have, then, this well-preserved, hard-working physician, aged seventy-five, who gives an extraordinary story of possible trauma to some organ in the upper abdomen. When I first glanced at this protocol I thought this might be quite simple and that we were dealing with a large abdominal aneurysm—a not too uncommon finding in people who have arteriosclerosis. I note in the record that the aortic pulsations were transmitted vigorously through this tumor, but nothing is said about lateral expansion, and I have to assume that it was not expansile. Also, from the size of the mass alone I think that one could feel quite sure that this was not an abdominal aneurysm. I have never seen an aneurysm so large as this, provided that this whole shadow, which is larger than a dinner plate in diameter, is the mass that is described. Therefore, I think I shall have to assume that this was probably not an aneurysm.

What sort of mass could develop over a period of eight years, known to be present for at least three years by the patient himself, and from what organ could it arise? One immediately thinks of the possibility of a large pancreatic cyst, which would fit the location quite well and conceivably might coincide with the history of trauma. In the beginning of this story one might try to associate these periods of vasomotor collapse with some pancreatic disturbance. On the other hand the tumor is not consistent with the type of pancreatic tumor that ordinarily produces such marked and transient changes in the vascular bed.

There is the possibility that this tumor became acutely enlarged from hemorrhage following additional trauma. On at least three occasions when he worked too hard or strained or injured himself, acute episodes occurred. Pressure from sudden enlargement before nature could adjust the vasomotor system might explain the attacks of syncope. There is the possibility that these periods of faintness and sweating, certainly the one associated with a definite lowering of the blood pressure, were associated with this "nonexciting" elec-

trocardiogram. I am not competent to pass on that, but I should rather expect that they had nothing to do with any change in the heart or in the heart muscle.

Other tumors in this region must be considered. The roentgenologist kindly points out that one can see through the tumor wall, which suggests that it might be cystic. He also points out that the spleen has a normal shadow in its proper position. The location of the mass is against its being a tumor of the spleen or liver. It is fairly centrally placed, whereas one would expect it to be more lateral if it arose from either of these organs. Therefore, I think we cannot expect it to be a cyst of the spleen, liver or kidney, but we must consider the possibility of a mesenteric cyst. Mesenteric cysts are not frequent but they do occur. They are painless to palpation unlike lymphomatous masses, which are always tender to palpation. They do have a tendency to produce some digestive symptoms on occasion. A cyst of the gastrosplenic mesentery, for example, could perfectly well displace the colon downward. There is perhaps some shadow here of the colon, which suggests that it has been pushed downward. I do not particularly see why the colon should have been pushed down into the pelvis by a pancreatic cyst, although an attachment could have been effected, possibly from an inflammatory process.

That is about as far as I can go. Obviously this was not considered to be an aneurysm. I shall choose as my first diagnosis a mesenteric cyst, and as a second choice a pancreatic cyst.

DR. BENJAMIN CASTLEMAN: How do you account for the three episodes that he had?

DR. ALLEN: Lots of people have episodes of collapse and fainting from one cause or another that are not easily explained, particularly people in this age group. But I accounted for it on the basis of sudden increase in the size of the tumor from hemorrhage into it, owing to injury, overwork or strain. This might have produced an increase in size that was too difficult for the vasomotor or sympathetic system to adjust immediately.

DR. CASTLEMAN: Dr. Sweet operated on this patient with a preoperative diagnosis of cyst of the omentum. Perhaps he will tell us more about it.

DR. RICHARD H. SWEET: It is too bad they accepted the house officer's physical findings, because I was certain that it was not a cyst. The patient's own diagnosis was cyst of the mesentery. To me, the mass felt like a solid tumor, although I did not know where it came from. It could be moved from side to side, but not into the lower abdomen.

When it was placed over the aorta, it transmitted pulsations readily; when it was taken off the aorta, pulsations could not be obtained. Since it would

narrow pedicle but by a broad base measuring at least 20 cm. across and 5 to 7 cm. deep. Of course, the tumor was removed. The patient left the

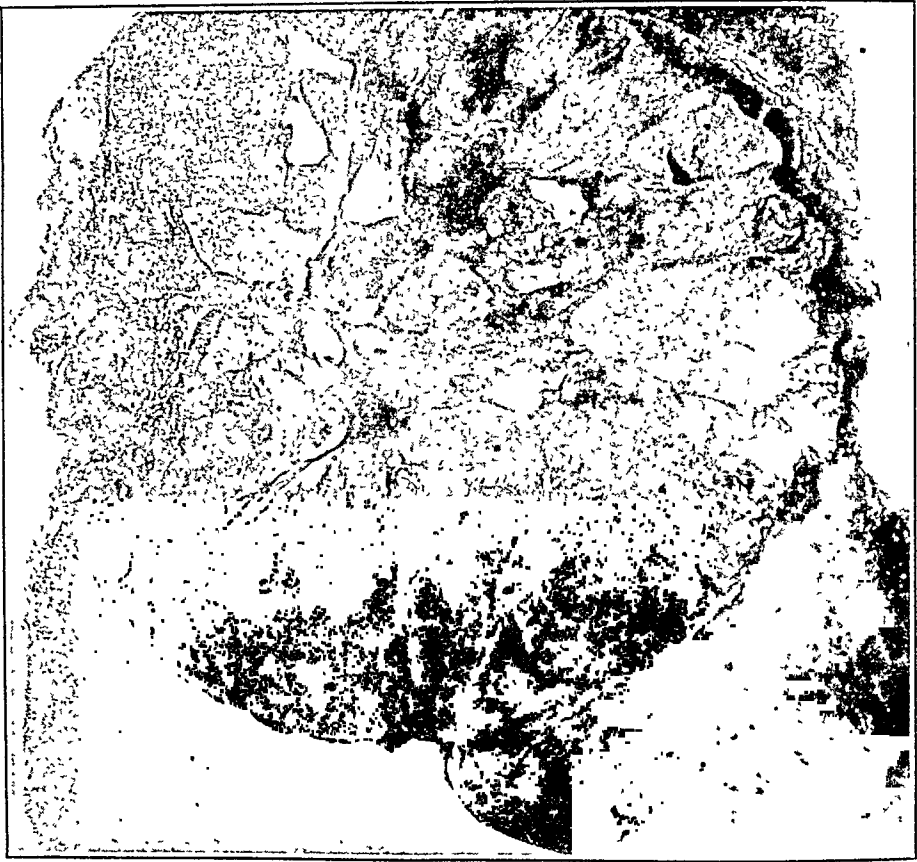


FIGURE 1. *Photograph of the Tumor.*

not go into the lower abdomen, I knew it was attached to something higher up.

Another point of interest was that when the patient had this collapse in the hospital I called in a member of the staff who had seen him during two or three similar episodes at home. He thought the attack was cardiac in origin. He could not give it a satisfactory name, but thought perhaps that it was a vagal reflex or something like that.

At operation the cause of the collapse was manifested as soon as the abdomen was opened—he had bled into the abdominal cavity. There was a large amount of blood within the abdomen, and it was just old enough to have been associated with the attack of three days before. The tumor was obvious, and I saw immediately that the hemorrhage had come from a soft spot in the tumor. There was a tremendous blood supply from the omentum, which had become adherent to the upper surface of the tumor. The vessels from the omentum were enormous and very fragile, as omental vessels are when they are dilated. The tumor was solid, arising in the left lobe of the liver; it was attached not by a

hospital on the fifteenth postoperative day and perfectly all right at the present time (one month later).

CLINICAL DIAGNOSIS

Cyst of omentum.

DR. ALLEN'S DIAGNOSIS

Mesenteric cyst?

Pancreatic cyst?

ANATOMICAL DIAGNOSIS

Hepatoma.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The tumor measured about 20 cm. in diameter and was nodular. As Dr. Swenson mentioned there was a necrotic focus on the surface, undoubtedly the source of the bleeding. The photograph (Fig. 1) is a cross section of the tumor showing that it is well circumscribed, with numerous yellowish-orange areas of necrosis, such as are not infrequently seen in renal-cell carcinomas. In fact, grossly, I thought that this pro-

bly was a metastasis from a renal-cell carcinoma. There was no evidence of cirrhosis in the surrounding liver tissue or of invasion of the hepatic veins—findings that are usually present in primary liver-cell cancer. Despite this, the tumor micro-

into the vena cava, metastasizing to the lungs. Dr. Schatzki* looked up a number of cases a few years ago and found that the average duration of life in the latter type is about six months.

DR. ALLEN: Was this in the right or left lobe?



FIGURE 2. Photomicrograph of the Tumor.

scopically is of liver-cell origin (Fig. 2), a very slowly growing hepatoma. We were unable to find any mitoses and classified it as a tumor of low-grade malignancy. Although the gross photograph shows that the tumor was completely encapsulated, a cross section at a deeper level revealed nodules of tumor in the liver parenchyma beyond the capsule. However, there was still a goodly margin of safety. When fixed in formalin, the tumor cells took on a greenish color, showing that they were forming bile.

It is interesting that this morning I was called to the operating room by Dr. Allen, who was operating on a girl with hemolytic jaundice. He removed the spleen and the gall bladder, which contained several gallstones, and then he found a nodule in the liver. He asked me whether he ought to resect it. I thought he should. We discussed the possibility of what it was, and he said that he thought it was a hepatoma.

DR. ALLEN: That is why it never occurred to me that this patient could have had a hepatoma.

DR. SWEET: Some of us have the impression that these tumors are usually very malignant. Is that so?

DR. CASTLEMAN: There are two types. The large solitary type can remain in the liver for years, with no untoward effects, and we occasionally find them incidentally at autopsy. Others are very malignant and spread via the hepatic veins

DR. SWEET: It was to the left of the falciform ligament. Grossly the remainder of the liver looked normal.

DR. ALLEN: Do you think that trauma had anything to do with the origin of this tumor?

DR. CASTLEMAN: No. I think that he had hemorrhage in the tumor because of the trauma.

DR. ALLEN: I mean at the time he was jostled in the automobile eight years before entry.

DR. CASTLEMAN: I believe that he already had the tumor at that time.

CASE 29332

PRESENTATION OF CASE

An eighty-nine-year-old physician entered the hospital because of change in mental state, aphasia and right-sided weakness of two days' duration.

The patient had been extremely active, busy and in apparent good health except for a dull "head" and occasional headaches during the previous year. Two days before admission he developed severe headache, unaffected by aspirin, and vomited several times. Vomiting was not projectile. On the afternoon of that day he fell on the way to the toilet, bruising his face. He was restless during the night, voided in bed and developed

*Schatzki, R. Roentgenological diagnosis of primary carcinoma of liver. *Am. J. Roentgenol.* 46:476-483, 1941

weakness of the right arm as well as generalized weakness. He was unable to stand up without aid. The blood pressure was said to have been 90 systolic, 50 diastolic, on one occasion, and 138 systolic, 90 diastolic on another. For the two days preceding entry the family noted gradually increasing mental dullness. He was slow in response to questioning and experienced difficulty in expressing himself until the time of admission, when he was unable to talk although he seemed to comprehend what was said to him. The restlessness had also increased.

At the age of eighty-four he was in the hospital for three days with the diagnoses of slight congestive failure and partial auriculoventricular block, associated with coronary heart disease. About six weeks before entry he fell, striking his head, nose, eye and ribs. The injuries were minimal and recovery seemed complete, although later examination showed a depressed fracture of the nose. It was not known whether the patient had been unconscious at that time. He had headaches off and on since.

Physical examination showed a semistuporous and restless man. There was a fresh hematoma on the right outer orbit that had apparently developed since the fall in the bathroom. The eyes looked forward in spite of efforts to make him look in other directions. The chest was barrel shaped and moderately fixed in expiration. The lungs were clear. The heart sounds were distant and of poor quality but regular. A questionable late diastolic murmur was heard over the precordium. There was definite weakness of the right arm. The lower extremities were essentially normal. A positive Babinski sign was obtained on the left. The tendon reflexes were bilaterally equal. He was unable to speak but seemed to recognize his surroundings. The neck was not stiff.

The blood pressure was 110 systolic, 74 diastolic. The temperature was 99°F., the pulse 70, and the respirations 23.

Urine examination showed an alkaline reaction with a + test for albumin. The white-cell count was 9000. The blood Hinton test was negative.

The following day the patient could not be aroused. He developed marked Cheyne-Stokes respirations, with blood pressures of 135 systolic, 80 diastolic, during hyperpnea, and 100 systolic, 60 or less diastolic, during apnea. There was no cyanosis or edema but occasional hiccups. The weakness of the right face and the arm appeared to be progressing.

An electrocardiogram revealed marked sinus arrhythmia, with a rate of 100 to 50 but with rela-

tively normal P, Q, R, S and T waves; the P interval was 0.2 second.

During the next three or four days the patient condition remained essentially the same, with perhaps slight progressive improvement. On the fifth hospital day he had fewer hiccups and seemed to recognize his friends but was still unable to speak. The blood pressure varied from 140 systolic, 90 diastolic, to 110 systolic, 80 diastolic.

During the next seven days he seemed to alternate between periods of drowsiness and alertness. When alert, he answered questions intelligently, recognized his friends and family and wanted to get up. He was unable to move the right arm or leg. There were no apparent sensory disturbances and no hemianopsia. It was not known whether he had any headache. The blood pressure ranged from 110 systolic, 75 diastolic, to 116 systolic, 100 diastolic.

On the fifteenth hospital day the patient became unresponsive. Respirations were rapid, with rales at both bases but without dullness. The temperature, pulse and respirations increased, and there was cyanosis of the lips and tongue. During the next two days, the respirations rose to 40, and he died on the seventeenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. G. COLKET CANER: The chief points in this case are as follows: The patient had a head injury, followed by headaches off and on for six weeks, and then a severe headache, which either preceded or followed another head injury—the history is not clear which came first. This severe headache was associated with vomiting. He then had increasing difficulty in expressing himself but seemed to understand. He also developed weakness of the right arm and became less responsive and finally comatose. After four days he improved.

In regard to location, the weakness of the right arm and the motor aphasia point to the left frontal parietal region, cortical or subcortical, as that is the greatest brain damage. A lesion in this region would affect the left cortical center for conjugate deviation of the eyes and would result in inability to turn the eyes to the right. The fact that the eyes could not be turned to either side suggests bilateral lesions. Bilateral lesions would also explain the fact that he had weakness of the right arm and aphasia and also a Babinski response on the left. However, the Babinski on the left can also be explained by an expanding left-sided lesion that caused pressure on the left cerebral peduncle by the edge of the tentorium. The rather rapid development of coma suggests rapidly increasing intracranial pressure affecting the mid-

brain. The hiccups might have been due to mid-brain or medullary compression secondary to generalized increased intracranial pressure.

The age of the patient, together with the fairly rapid development of coma, suggests a vascular lesion and the history is rather typical for subdural hematoma. It is well known, of course, that subdural hematomas may follow minor head injuries, particularly if arteriosclerosis has diminished the elasticity of the blood vessels. It is well known, too, that a hematoma is frequently found on both sides of the brain, and as I have said, there is reason to suspect bilateral lesions in this case. A subdural hematoma would explain the intermittent headache for six weeks following the first head injury, and it would account for the severe headache and other symptoms whether or not they began before or after the second head injury. It would also explain the rapidly increasing coma without extension of the paresis. In fact I see nothing in the record that cannot be easily explained by this diagnosis. It seems to me that, with a history of this kind, burr holes are indicated. When a subdural hematoma is a possibility there is much more to be gained by this procedure than there is to lose.

The other possibilities are cerebral thrombosis, intracerebral hemorrhage, subarachnoid hemorrhage, and tumor with hemorrhage or acute edema around it.

I think thrombosis is the least likely because it does not explain the headaches for six weeks and because one would expect that a thrombosis large enough to cause coma would cause a hemiplegia and probably a hemianesthesia and hemianopsia, whereas the patient only had aphasia and weakness of the arm and face.

Intracerebral hemorrhage also seems unlikely. The onset would have been more rapid if there had been a hemorrhage. This is also true of subarachnoid hemorrhage, which, in addition, would probably have resulted in a stiff neck. The history seems much more suggestive of a vascular lesion than of tumor, although tumor with hemorrhage into it cannot be ruled out.

Finally, I see no relation between the patient's cerebral symptoms and the heart disease that necessitated hospitalization five years previously, except that arteriosclerosis was probably a factor in the development of the subdural hematoma and seems to have been the cause of the heart disease. I think an electroencephalogram would have been more useful than an electrocardiogram. My diagnosis, therefore, is subdural hematoma, probably bilateral, with general arteriosclerosis and terminal bronchopneumonia.

DR. HENRY R. VIETS: Was a lumbar puncture done?

DR. CHARLES S. KUBIK: No.

DR. VIETS: That might have thrown more light on the problem.

DR. KUBIK: Dr. Ayer, would you like to make any comment?

DR. JAMES B. AYER: It was thought best, because of the patient's eighty-nine years, to do as little as possible; so that even a lumbar puncture



FIGURE 1. Photograph of the Superior Surface of the Brain Showing Marked Depression on the Left and Slight Depression on the Right

was not done. Encephalograms were impractical. It was suggested that the lesion was a subdural hematoma and that possibility was held to. However, even if it was a subdural hematoma, it was thought that the patient would not stand operation and radical treatment was therefore not pushed. The improvement in the week before he died was so striking that thrombosis seemed more likely.

CLINICAL DIAGNOSIS

Cerebral thrombosis?

Subdural hematoma?

DR. CANER'S DIAGNOSES

Subdural hematoma, bilateral.

Generalized arteriosclerosis.

Bronchopneumonia, terminal.

ANATOMICAL DIAGNOSES

Subdural hematoma, bilateral.
 Calcific aortic stenosis.
 Cardiac hypertrophy.

PATHOLOGICAL DISCUSSION

DR. KUBIK: There were bilateral subdural hematomas, as Dr. Caner suspected. That on the left side was considerably larger, although the encapsulating, rather dense, fibrous membranes were of the same thickness and presumably of the same

the larger hematoma was situated (Figs. 1 and 2). Although a marked cerebellar pressure cone did not exist, there was a deep groove across the medulla where it rested against the anterior margin of the foramen magnum. Thus there was evidence of medullary compression, which presumably accounted for the respiratory difficulty.

DR. VIETS: Did the tentorium cut in enough to account for the positive Babinski sign on the left?

DR. KUBIK: Apparently not, although that is a fairly common occurrence with subdural hema-

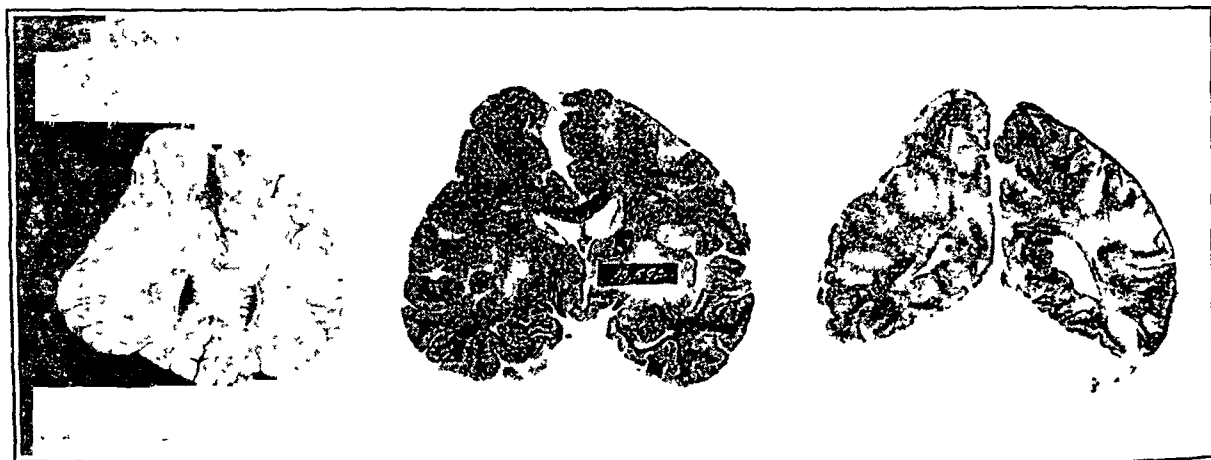


FIGURE 2. Photograph of Cross Sections of the Cerebral Hemispheres Showing Marked Depression on the Left and Slight Depression on the Right.

age. Both hematomas consisted almost entirely of dark purplish-red fluid, which escaped when the dura was incised; there was little organized or unorganized blood clot. The spaces occupied by the hematomas were completely surrounded by fibrous membranes—an outer one that was adherent to but easily stripped from the inner surface of the dura, and an inner one that lay between the hematoma and the arachnoid membrane, to which it was not adherent. These encapsulating membranes are fibroblastic structures derived from the dura.

There was characteristic depression by the hematomas of the surfaces of the cerebral hemispheres, much more pronounced on the left side, where

toma; the midbrain may be displaced so far to the opposite side by a temporal pressure cone that the contralateral cerebral peduncle is forced against the margin of the tentorium. An actual groove across the peduncle may result. By implication of the corticospinal tract above its decussation, a homolateral hemiparesis or hemiplegia occurs. In this patient, the bilateral signs can probably be explained by the bilateral lesions.

DR. BENJAMIN CASTLEMAN: The heart was slightly hypertrophied, weighing 450 gm. This was apparently due to a marked calcific aortic stenosis. The coronary arteries showed a moderate degree of atherosclerosis but no appreciable narrowing.

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UNITED STATES CADET NURSE CORPS

It is well known, particularly by physicians, that the war effort has created a serious shortage of nurses. During the current year, it is estimated that 65,000 new student nurses must be enrolled if the essential military and civilian nursing services are to be fully covered, and to assist in meeting this need, Congress has recently passed the Bolton Act, which creates the United States Cadet Nurse Corps.

In essence, the act provides for grants-in-aid to nursing schools whereby the student nurse is relieved of the burden of tuition and other fees and expenses that she would ordinarily

herself and, in addition, is paid a small monthly stipend. The student is permitted to enter the nursing school of her choice, provided that it is participating in the program and that she is able to meet its scholastic, personal and physical requirements. Furthermore, any student nurse who enrolled in a participating school subsequent to January 1, 1941, is eligible to join the corps. The cadet must agree, however, to engage in essential nursing—military or civilian—for the duration of the war. For the nursing schools, certain broad requirements are specified regarding minimum standards of nursing education and acceleration of the training program. Additional information concerning the new program is contained in a short article by Surgeon General Thomas Parran in the July 10 issue of the *Journal of the American Medical Association*, and details may be obtained from nursing schools, state nursing councils or associations and the Division of Nurse Education, United States Public Health Service, Washington, D. C. Recruitment of student nurses has encountered severe competition from the many opportunities available at present to high-school graduates, especially in the uniformed services and in war industry, where pay is immediate, and it is hoped that this legislation will aid in meeting the competition and will thus result in appreciable numbers of student nurses.

The family physician can do a great deal to support this worthy program. It is only natural that young women who contemplate joining the Cadet Nurse Corps should turn to him for advice and guidance. In pointing out to the prospective nurse some of the reasons why she is needed and how she will benefit herself and her country, the physician on the home front will make still another patriotic contribution to the prosecution of the war. Furthermore, it is to his own interest to stimulate recruitment, since, as his load of work becomes heavier, nurses can be of increasing assistance to him. In fact, all physicians are urged to utilize every means to encourage young women to accept this new opportunity to aid in meeting

THE FIRST COLLEGE TEXT IN OPTICS

THE long-delayed renaissance in medicine, which even lasted through the seventeenth century, is well illustrated by the first college text in optics, published in London in 1651. The author, Thomas Powell, a Welshman, was, it is true, not a physician but an erudite Doctor of Divinity at Oxford. His book, *Elementa Opticae Nova*, nevertheless, must have been widely read for only two copies seem to have survived, one in the British Museum, and the second recently acquired by the Dartmouth College Library. In his description of the Dartmouth copy, Burian* points out that Powell only compiled the opinions of the philosophers and poets of the Greco-Roman period, ignoring the writings of his own time. His anatomy of the eye is based entirely on Galen's description, the lens being placed in the center of the eyeball, although Fabricius ab Aquapendente had described it properly in 1600. Powell considered the lens as still the main receptor organ in the eye, in spite of the fact that Kepler and others had already considered its function as a purely dioptric one. The author also listed seven extraocular muscles, although in the sixteenth century Fallopius had correctly described six. Powell, therefore, did not go beyond Euclid and Ptolemy and depended heavily on Aristotle.

Thus science was delayed. The ophthalmologic student of 1651 in England had only this book to use, and thus his outlook was turned back at a time when Harvey and his few contemporaries were moving forward against the strong tide. However, the tide was ebbing, and before long Powell and his static science were to be finally overcome by Leeuwenhoek, Boerhaave, John Taylor and particularly William Porterfield and Thomas Young.

Powell, in his missionary zeal to keep the world clean, was disgusted with what he describes as "paradoxes and monstrous new opinions." He

could not stomach the "demented and eccentric ambition" to "attain a new Medicine, a new Philosophy." Men of his type, as pointed out by Burian, kept the teachings of men such as Kepler waiting for well over a century before they became the common property of even the men of science.

MEDICAL EPONYM

BESNIER-BOECK-SCHAUMANN DISEASE

On February 14, 1889, Dr. E. M. Besnier (1831-1909), physician of the *Hôpital Saint-Louis*, presented at a meeting of the physicians of that hospital a case of *lupus pernio de la face*. This case report appears in *Annales de dermatologie et de syphiligraphie* (Second Series, 10: 333-336, 1889). A portion of the translation follows:

A kind of erythematous lupus of the face in the form of erythema pernio or local asphyxia, for which I propose the designation lupus pernio, or asphyxial lupus, allied to Hutchinson's chilblain lupus, but not quite identical.

Ten years later, Caesar Peter Moeller-Boeck (1845-1917), professor of dermatology and syphilis at Oslo, published an article entitled "Multipelt benign hud-sarcoid [Multiple Benign Sarcoid of the Skin]," which appeared in *Norsk magasin for lægevidenskapen* (60: 1321-1334, 1899). After referring to clinical accounts of similar lesions, he concludes as follows:

The above described tumor, which so far as I know is here studied for the first time, at least histologically, thus seems clinically and histologically to occupy an independent position, and on the basis of the histologic findings I have ventured to designate it provisionally as "multiple benign sarcoid."

The possibility exists that further study may demonstrate it to be related to the pseudoleukemias.

Dr. Jörgen Schaumann, of Stockholm, published a paper "Etude sur le lupus pernio et ses rapports avec les sarcoides et la tuberculose [Study of Lupus Pernio and Its Relation to Sarcoids and Tuberculosis]" in *Annales de dermatologie et de syphiligraphie* (Fifth Series, 6: 357-373, 1917). Following a reference to Dr. Besnier's case, he concludes:

Lupus pernio and cutaneous sarcoids are symptoms of one and the same disease.

This disease is a tuberculoid lymphadenopathy characterized by the multiplicity of its lymphatic distribution in the lymph nodes, the tonsils, the bone marrow, the lungs, the spleen and the liver.

*Burian, Hermann M. A text for the times of Cromwell. *Dartmouth College Library Bulletin* 4 19 24, 1943.

WAR ACTIVITIES

FOOD RATIONING

The following statement, reprinted from the July 17 issue of the *Journal of the American Medical Association*, is a summary covering recent amendments in the regulations governing food rationing.

The Office of Price Administration announced on July 2 that any medical practitioner authorized by the state in which he practices to prescribe all internal drugs is also authorized to certify that a person requires supplementary food rations for health reasons. Authority to make such certification was previously confined to doctors of medicine. OPA has now broadened the authority so that osteopaths in states which license osteopaths to prescribe all internal drugs may also prescribe supplementary food rations. Food rationing regulations provide that a person whose health requires more rationed food than his ration points permit him to buy may apply to his local board for necessary additional points. In some instances foods are prescribed in addition to drugs or medicines or as a substitute for them. In some counties the work of ration boards in processing such applications has been much simplified through the voluntary help of the doctors themselves. By establishing panels to review all medical certifications and to advise the boards responsibility for issuing extra rations for health reasons has been kept on a professional level.

OPA, under date of June 1, placed evaporated and condensed milk on the list of rationed products. These types of milk are added to the group of rationed foods containing meats and fats, for which red ration stamps are needed without any increase in the total number of points allowed for this group. One point is required for one 1½-ounce can or for two 6-ounce cans or for two 8-ounce cans. This means that the child may use 7 of his 16 points per week for his milk requirements in terms of evaporated milk which allows slightly less than the equivalent of a quart of whole milk per day and have 9 points remaining for his meat and fat requirements. An invalid or any other person whose health requires that he have more canned milk than he can obtain with the stamps in his ration book may apply at his local ration board for additional points. The consumer must submit a written statement of a licensed physician showing why he must have more canned milk, the amount needed during the succeeding two months and why unrationed foods cannot be used instead. A supplemental allotment to acquire canned evaporated and condensed milk needed by a hospital to meet the dietary needs of its patients may be obtained on application to its local ration board. It is understood that if the present method of rationing does not make evaporated milk available in all areas for infants and children, some more effective method will be worked out.

OPA has issued an amendment to Ration Order 16 (Amendment 25), which permits the use of rationed fats and oils for external therapeutic purposes. This includes the use of vegetable oils, such as cottonseed oil, for bathing newborn infants, for external application in skin diseases for urethral injection or lubrication of urethral instruments and for x-ray visualization. Such use of rationed fats and oils is defined as 'industrial consumption' and persons using these products for such purposes are classified as 'industrial consumers.' An industrial consumer engaged in the care and treatment of the sick and needing rationed fats and oils for this purpose may apply to his district OPA office for a certificate with

which to acquire them. The procedure to be followed, briefly, is as follows. The application should be made on Form R 1605 to the district office. If the applicant is a hospital the district office will pass on the application by using the same method of computing allowances as the local boards use in computing allotments for industrial users, otherwise the application will be forwarded to the Washington office for action. If the applicant requires more than he would receive by the method of computation described he should also submit Form R 315 stating the reasons for such request. An industrial consumer to whom a certificate is issued for 'industrial consumption' of rationed fats and oils may use it only to acquire the foods for which application was made and may use those foods only for the purpose for which the application was granted.

For several months OPA and medical authorities have been studying the hospital problem with a view to developing a uniform procedure covering the granting of supplemental allotments for hospitals. Solution of the problem is believed near. In the meantime a provision in the regulations (Ration Order 5, Section 116) should enable hospitals to obtain the necessary supplemental allotments so that patients need not suffer from dietary deficiency. This provision gives local boards authority to grant such allotments to meet the dietary requirements of patients living in and receiving care in hospitals whether or not such patients are on special diets. In determining the amount of the supplemental allotment for processed foods and the commodities covered by Ration Order 16, the local board will take into consideration the availability of fresh fruits and vegetables, unrationed substitutions, such as poultry and fresh fish, and the physical facilities of hospitals to process and store such foods.

NEW HAMPSHIRE MEDICAL SOCIETY

FRENCH—EDWARD H. FRENCH, M.D., of Wollaston, Massachusetts died May 4. He was in his eighty-seventh year.

Dr. French graduated from Dartmouth Medical School in 1892. He was a member of the staff of the New Hampshire State Hospital from 1893 to 1896 and superintendent of the Medfield, Massachusetts State Hospital from 1896 to 1917. Dr. French, as a member of the New Hampshire Medical Society, received a gold medal in recognition of his fifty years of membership in 1935.

MISCELLANY

THE FAMILY DOCTOR, THE PATIENT AND THE JOB

The first step in the rehabilitation of a tuberculous person is physical restoration, which is particularly the province of the physician. In the further adjustment of the inactive patient the lay worker who attempts to serve the patient without learning the story of diagnosis, treatment and recovery from the physician, treads on quicksand. Most successful rehabilitation follows the concerted application of the medical skill of the physician and the special information and training of qualified lay workers. Practical suggestions for the family physician who is interested in such co-ordination are here presented by Dr. F. L. Jennings, superintendent and director of the Sunnyside Sanatorium, Indianapolis, Indiana.

The private physician who has guided his patient through recovery from pulmonary tuberculosis is now

being asked frequently to advise concerning some job which that patient may attempt without too great hazard. In this general manpower shortage, the patient with inactive tuberculosis, whether from civilian life, from induction centers or discharged from military services, can find employment readily in many localities, particularly if he has an established skill. Besides that economic need which makes many patients reluctant to continue treatment for the prescribed period, patients now are moved by the wish to become a part of the war effort and sometimes by high wages. Some employers who hire all comers are unlikely to establish any safeguards for handicapped workers.

One of the physician's paramount difficulties has been the item of sufficiently definite information about the job in question. Jobs are changing rapidly. The exhausting task of a year ago has been reduced to machine-tending. Redesign, retooling, reorganization and re-routing continue to make more specifications obsolete. Keeping up with such rapid and drastic change is impossible alike for any physician or lay worker without current sources of industrial information. Some physicians have sought to bridge this difficulty by such general terms as "light work," hoping thereby to protect the patient from excessive exertion, strain and tension. Unfortunately, employers' requirements are definite. Employment placement interviewers must meet these definite requirements. A patient's ability to do "light work" is indefinite and unsalable.

But there are now official and unofficial sources of information through which physician and patient may usually find definite indications concerning which job is free from undesirable hazards. The official services include the United States Employment Service, which has branch offices in most population centers, and the state vocational rehabilitation services. The United States Employment Service has the most complete and currently accurate information on what jobs there are in each community and on what physical performance is required in each job. It has originated a "Physical Demands Form," which is being used experimentally to determine required physical activity and working conditions. This type of job analysis explores especially such items as continuous standing, sitting, lifting, stooping and so forth. One purpose of this information is to check the specific requirements of the job against the specific limitations of the handicapped applicant.

Interested physicians may obtain copies of interim physical requirement forms from the National Tuberculosis Association. The larger offices of the United States Employment Service also include executives or interviewers who have some experience in special placements and who are qualified to discuss the subject of suitable placement for recovered patients with their physicians. The service has placed thousands of inactive tuberculous patients in hundreds of different jobs. The suitability of these placements has depended most of the time on the quality and quantity of medical information available.

When the recovered tuberculous patient has no marketable skill, or when his old job is contraindicated medically, application for training or retraining and placement should be made to the state bureaus of vocational rehabilitation. Financed by state appropriations and federal matching funds, these bureaus are empowered to impart specific vocational training and placement to handicapped adults in order to make them self supporting.

The physician will find in federal Form R-3a (revised), published by the Federal Vocational Rehabilitation Bu-

reau and in the manual prepared for its interpretation (Misc. 2328) practical bases on which rehabilitation agent and physician may cohere their services for the patient. The form and the manual are the result of many consultations between federal rehabilitation personnel and members of the Council of the American Trudeau Society and other phthisiologists of long experience. Many state agents and supervisors have learned that, as the federal manual points out, direct interview between physician and rehabilitation worker is the most satisfactory procedure for both.

A number of the state and local tuberculosis associations have included rehabilitation in their program objectives. Some have employed special personnel competent to assist the patient in finding his way to appropriate training or placement or both. Rehabilitation workers employed by voluntary agencies are well aware that the patients of private physicians may have as much need for their services as the sanatorium graduate. The physician may find it well worth while to inquire from the nearest tuberculosis association what it has to offer in the direction of rehabilitation.

Both official and voluntary resources have been stimulated and encouraged by changing attitudes within industry. Not manpower shortage alone, but a cumulation of satisfactory performance by former patients, has done much to improve this situation.

The nation's leading personnel agency, the United States Civil Service Commission, has conducted surveys of jobs in several types of federal services and in war-contract industries in search of jobs suitable for physically handicapped persons. Prospective employment for persons with a history of tuberculosis has been conspicuously included.

This precedent has been matched by action on the part of the National Association of Manufacturers. In the December, 1942, supplement of its *Industrial Relations Bulletin*, the association indicated that various handicapped groups are a new labor source. Specific mention is made of employees who have suffered amputations, deafness, blindness, organic heart disease and tuberculosis. For each group, a partial list of suggested jobs is offered. The bulletin indicates that one of the parallel practices in employing handicapped workers calls for "careful selectivity in applying the handicapped man to a job which he can do." Again the private physician and the industrial doctor are able to provide medical advice and counsel. A number of large employers have recently utilized the specific job-analysis method developed by the United States Employment Service, described above.

Tuberculosis literature is not without its contributions on rehabilitation information of value to the physician. The *American Review of Tuberculosis* has in preparation articles prepared by the United States Employment Service and the Federal Vocational Rehabilitation Bureau regarding their procedures in cases eligible for their services. The Rehabilitation Service of the National Tuberculosis Association is preparing special releases on the subject of patients not eligible for official services. Thus, the physician, when called on to advise his patient occupationally, may utilize the services and the publications of the United States Employment Service, the rehabilitation bureaus and the tuberculosis associations to good advantage. — Reprinted from *Tuberculosis Abstracts* (August, 1943).

(Notices on page xii)

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THE EFFECT OF VITAMIN K₁ OXIDE ON HYPOPROTHROMBINEMIA INDUCED BY DICOUMAROL*

CHARLES S. DAVIDSON, M.D.,† AND HARRIET MACDONALD, B.S.‡

BOSTON

MUCH attention has recently been given to the use of dicoumarol as an anticoagulant. The advantages of the drug over heparin, such as oral activity and relatively low cost, are apparent, but the serious disadvantage of lack of control has been given less attention.¹ Overman et al.² point out that in rats vitamin K has an action antagonistic to that of dicoumarol. Shapiro et al.³ gave small doses of dicoumarol to patients and found that the combined oral and parenteral administration of large amounts of 2-methyl-1,4-naphthoquinone—a synthetic compound similar to vitamin K—prevented the prolongation of the prothrombin time following the administration of dicoumarol.

It seemed advisable to determine whether vitamin K has any influence on the action of dicoumarol given in therapeutic doses. It was evident that very large doses of the vitamin would be required because usual doses, or even those ordinarily thought to be large, have been shown repeatedly to be ineffective.⁴⁻⁷ An occasional report concerning the control of large doses of dicoumarol by vitamin K has appeared in the literature.⁸

Fieser⁹ and Seligman et al.¹⁰ have pointed out that the synthetic compound 2-methyl-1,4-naphthoquinone differs greatly, both chemically and physiologically, from true vitamin K₁ or K₂. Furthermore, it is known that this compound has produced toxic effects in small animals.¹¹ Therefore it seemed inadvisable to administer large doses to patients.

True vitamin K₁ oxide,§ synthesized by the

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‡Laboratory assistant, Thorndike Memorial Laboratory, Boston City Hospital.

§The vitamin K₁ oxide was kindly supplied by Dr. Arnold Seligman, of the Peck Israel Hospital, Boston, and by Merck and Company, Rahway, New Jersey.

method of Fieser¹² and prepared for use as suggested by Davis et al.¹³ was employed in this investigation. The amount of vitamin K₁ oxide was accurately measured either volumetrically or by weighing. The latter method is probably more accurate. From 100 to 450 mg. of vitamin K₁ oxide in oil form was dissolved in 15 to 20 cc. of absolute alcohol. The resulting solution was poured slowly, with sterile precautions and constant agitation, beneath the surface of 1000 to 1500 cc. of 5 or 10 per cent glucose in water. A fine suspension of the vitamin was thus obtained. The patients received by intravenous administration 1000 to 1500 cc. of this preparation. The time of administration varied from three to five hours. No serious untoward effects were noted. Two patients complained of headache and 1 vomited following the injection. The amount of alcohol administered produced no untoward effect except the production of a mild euphoria in some patients.

The dicoumarol|| was used in the form of the crystalline compound and administered orally in gelatin capsules.

The prothrombin times were determined by a modification¹⁴ of the method of Quick.¹⁵

RESULTS

The effect of the administration of vitamin K₁ oxide on the hypoprothrombinemia produced by dicoumarol was studied in 5 patients. Two methods of attack were used. In one an attempt was made to prevent dicoumarol from having its customary hypoprothrombinemic effect. In the other the full effect of dicoumarol was permitted to occur and vitamin K₁ oxide was then administered in an attempt to bring the prothrombin concentration back to normal.

Figure 1 demonstrates the preventive action of 180 mg. of vitamin K₁ oxide on the effect of di-

||The dicoumarol was kindly supplied by the Abbott Laboratories, North Chicago, Illinois.

coumarol administered orally in a dose of 500 mg. Following the administration of the dicoumarol, the patient's prothrombin time rose from a normal value of twenty-eight seconds to a maximum of fifty seconds two days after the administration of the drug. Twelve days later a second dose of 500 mg. of dicoumarol was administered. Five hours later the intravenous injection of vitamin K₁ oxide was commenced and 180 mg. was administered in the next two hours. As shown in the figure there was no significant change in the prothrombin time of this patient when the vitamin K₁ oxide and dicoumarol were administered in the doses and under the conditions described above. After a lapse of twelve days, a third dose of 500 mg. of dicoumarol was administered without the simultaneous administration of vitamin K₁ oxide.

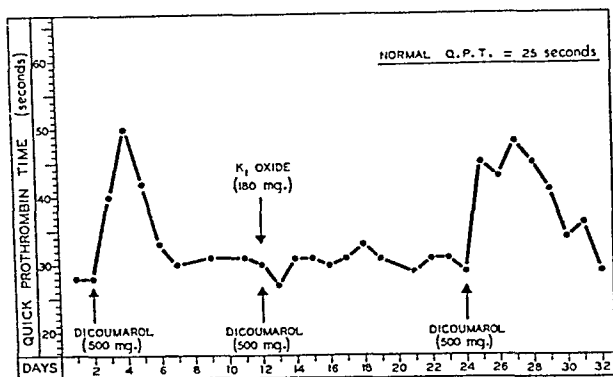


FIGURE 1. *The Preventive Action of Vitamin K₁ Oxide on the Hypoprothrombinemia Induced by Dicoumarol.*

The response to the dicoumarol was prompt and the usual hypoprothrombinemia resulted. It should be noted that following the first administration of dicoumarol five days elapsed before the prothrombin level returned to normal, and following the third administration a period of eight days was required to obtain this result.

Figure 2 demonstrates the effect of the administration of vitamin K₁ oxide on the hypoprothrombinemia obtained following the administration of dicoumarol. In this patient 500 mg. of dicoumarol was insufficient to produce a marked hypoprothrombinemia, and a second dose of 1 gm. of the drug was therefore administered three days later. The prothrombin time rose from a normal value of 25 seconds to 55 seconds in a period of two days. At that time, 250 mg. of vitamin K₁ oxide was administered intravenously. A prompt reduction in the prothrombin time occurred. In four hours it fell to 35 seconds, and in twelve hours to 31 seconds, and in twenty-four hours it returned to its original normal value. Four days after the prothrombin time was normal, a second dose of 1 gm. of dicoumarol was administered,

with a consequent rise in prothrombin time from 25 seconds to 75 seconds over a period of two and a half days. However, six and a half days elapsed before the prothrombin time returned to normal, in sharp contrast to the rapid reversal of the hypoprothrombinemia observed when vitamin K₁ oxide was administered. This important difference in rate of return is demonstrated more

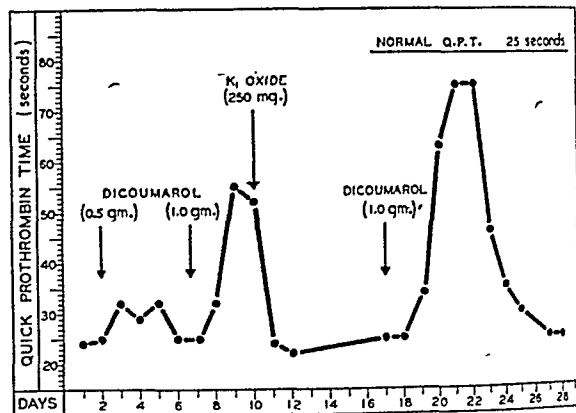


FIGURE 2. *The Antagonistic Action of Vitamin K₁ Oxide on Dicoumarol.*

clearly in Figure 3, in which the fall of the prolonged prothrombin time produced by dicoumarol, with and without the administration of vitamin K₁ oxide, is plotted in hours.

Three other patients were studied with respect to the action of vitamin K₁ oxide after the hypoprothrombinemia from dicoumarol had been established. The dose of dicoumarol used varied from 500 mg. to 1 gm. In 2 patients vitamin K₁ oxide was administered in a dosage of 350 and 450 mg., respectively, in two doses. In one of these

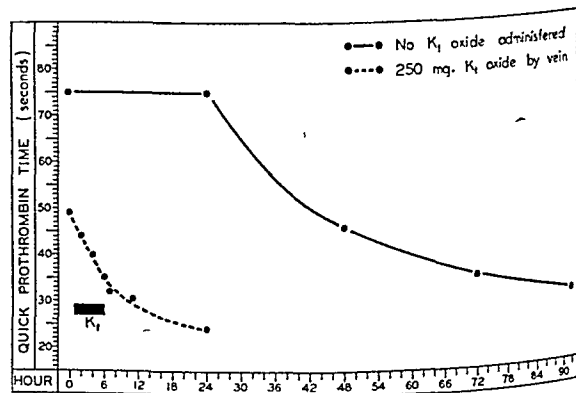


FIGURE 3. *The Effect of Vitamin K₁ Oxide on the Hypoprothrombinemia Induced by Dicoumarol.*
This is a portion of the curve shown in Figure 2, with the readings plotted in hours instead of days.

patients the prothrombin concentration returned to normal in fourteen hours, and in the other in twenty-four hours. The third patient was given

200 mg. of vitamin K₁ oxide after the hypoprothrombinemia had been established, without significant effect. Unfortunately, it was impossible to make further studies on this patient, but probably the dose administered was too small.

DISCUSSION

In 4 of 5 patients studied, the administration of vitamin K₁ oxide in large doses either prevented or reversed the hypoprothrombinemia produced by suitable doses of dicoumarol. Just as with the anticoagulant effect of dicoumarol, the amount of vitamin K₁ oxide required to produce an antagonistic effect varies from patient to patient and repeated doses of the vitamin may be necessary to secure the desired result. The quantitative relation between dicoumarol and vitamin K₁ oxide requires further study. Furthermore, it should be noted that the effect of vitamin K₁ oxide presented in this paper is confined exclusively to its effect on the hypoprothrombinemia produced by a single dose of dicoumarol. It will be necessary, therefore, to establish the usefulness of the vitamin as a means of controlling the coagulation time in patients who are receiving a prolonged course of dicoumarol. If, under these circumstances, it can be established that vitamin K₁ oxide acts in a similar fashion to that obtaining for a single dose of dicoumarol, it would seem likely that many of the dangers following the use of this anticoagulant can be removed.

SUMMARY AND CONCLUSIONS

The activity of large doses of vitamin K₁ oxide in reversing the hypoprothrombinemia produced by dicoumarol has been demonstrated in 3 out of 4 patients studied. It is probable that an inadequate amount of the vitamin was administered to the fourth patient.

In 1 patient, the administration of vitamin K₁ oxide prevented the subsequent establishment of a hypoprothrombinemia following the administration of dicoumarol.

The amount of vitamin K₁ oxide required to produce the desired effect varied considerably from patient to patient.

No serious toxic manifestations were observed from the administration of large amounts of vitamin K₁ oxide. The only untoward action observed in this small series of patients was transient headache and, in 1 patient, vomiting.

It is suggested that the action of vitamin K₁ oxide in reversing the hypoprothrombinemia established by single doses of dicoumarol may make the therapeutic use of this anticoagulant safer than it has heretofore been.

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CARDIAC ARRHYTHMIAS FOLLOWING PNEUMONECTOMY*

C. CABELL BAILEY, M.D.,† AND REEVE H. BETTS, M.D.‡

BOSTON

AURICULAR flutter and auricular fibrillation may occur as functional disturbances in cases in which no definite evidence of heart disease is present.¹⁻¹⁴ Ritchie² and others^{3, 4} as early as 1914 observed that flutter sometimes occurred when there was no evidence of heart disease. Parkinson and Bedford⁵ reviewed 52 cases of flutter and discovered 5 patients who had no detectable heart disease. Orgain, Wolff and White,¹ in reviewing 5000 cardiac consultation cases, found that 36 (6 per cent) of 583 cases of fibrillation and 5 (14 per cent) of 38 cases of flutter occurred when no detectable heart disease was present. This indicates the rarity of these two conditions, especially functional auricular flutter. The purpose of this paper is to emphasize the relative frequency of cardiac arrhythmias, especially functional auricular fibrillation and flutter, following pulmonary resection.

In a series of 78 patients on whom total pneumonectomy was performed at the New England Deaconess Hospital, 4 cases of auricular fibrillation, 2 cases of auricular flutter, 1 case of flutter-fibrillation and 1 case of nodal tachycardia were encountered postoperatively. An additional case of auricular fibrillation was observed following a right middle and lower lobectomy. The right lung was removed in 3 cases, and the left lung in 6 cases. The patients' ages varied from thirty-two to sixty-six years. There were 6 males and 3 females. No history of rheumatic fever or syphilis was elicited. All patients except one (Case 4) had negative blood Hinton tests. One had a slight elevation of the systolic blood pressure (160 mm.), which later dropped to normal.

X-ray films taken at six feet revealed cardiothoracic ratios well below 50 per cent in all cases. Five patients had normal preoperative electrocardiograms. Careful history-taking and physical examination failed to reveal evidence of heart disease in any case before operation.

The arrhythmias appeared on the second, third (2 cases), fifth, seventh, fourteenth and fifteenth days following pneumonectomy. In Case 6, flutter followed left pneumonectomy by twenty-nine days and pericardiostomy for a sterile pericarditis

by only one day. In Case 9, fibrillation followed pneumonectomy by fifty-seven days and thoracoplasty by ten days. That the procedures mentioned precipitated the arrhythmia in Cases 6 and 9 is probable. In 8 cases normal sinus rhythm was restored within forty-eight hours by rapid digitalization. In Case 7 there were two transient attacks of auricular fibrillation; one ceased spontaneously, and the other thirty minutes after a test dose of 3 gr. of quinidine sulfate. The duration of the arrhythmias in 7 cases was between thirty and forty-eight hours. The remaining 2 cases, both of fibrillation, lasted two and ten hours, respectively.

A follow-up of these 9 cases in December, 1942, varying from eight months to five years after the arrhythmia, revealed that no patient had developed cardiac decompensation or had had a return of the cardiac arrhythmia.

CASE REPORTS

CASE 1. T. K., a 45-year-old housewife, was admitted on December 29, 1936, complaining of chronic cough for 4 years and occasional blood-streaked sputum for 2 years. In 1934 she had a paroxysm of tachycardia of 2 hours' duration. In November, 1936, bronchoscopy and biopsy showed carcinoma in the left main-stem bronchus. Pneumothorax was given.

Physical examination was negative except for left pneumothorax and slight clubbing of the fingers. The usual laboratory findings were negative except for a white-cell count of 22,950. X-ray study showed a left pneumothorax with atelectasis of the left upper lobe. The cardiothoracic ratio was less than 50 per cent. An electrocardiogram was normal except for a tachycardia of 108.

On January 5, 1937, a one-stage left pneumonectomy was done. The course was satisfactory until the 19th postoperative day, when the pulse suddenly rose to 172. It was regular and not changed by carotid or ocular pressure. The patient was conscious of the tachycardia but was not distressed. An electrocardiogram showed a nodal tachycardia with a ventricular rate of 170. Eighteen grains of digitalis was given in the first 24 hours, the first 3 gr. intramuscularly and the rest by mouth. Thereafter 1½ gr. was given daily until February 5, when the digitalis was discontinued. The pulse remained rapid and regular for 48 hours, when it returned to a normal rhythm at 110. An electrocardiogram showed a normal sinus rhythm with a rate of 116.

When examined 4 years after the operation, she stated that she had been free from symptoms except for a moderate pulmonary hemorrhage 1 year previously.

CASE 2. S. S., a 43-year-old Syrian saleswoman, was first seen on March 14, 1938, complaining of intermittent hemoptysis for 1 year and an almost continuous vague discomfort in the left lower anterior chest for 11 months. The latter was not related to exercise or excitement.

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The only abnormality in the physical examination was diminished breath sound in the left axilla. Routine laboratory tests were negative. X-ray study showed atelectasis in the lower part of the left upper lobe. The cardiothoracic ratio was less than 50 per cent. A bronchogram showed obstruction of the lingular branch of the left upper lobe bronchus. Preoperative pneumothorax was then begun.

On April 11, a left total pneumonectomy was performed, two 500-cc. blood transfusions being given. The pathological report was adenocarcinoma of the left upper lobe. The patient did well until the 7th postoperative day, when she developed a sudden tachycardia of 170. She perspired and the skin felt clammy, but there were no other symptoms. An electrocardiogram showed auricular fibrillation, with a ventricular rate of 150. Twelve grains of digitalis was given in the first 12 hours and $1\frac{1}{2}$ gr a day thereafter for 10 days. Thirty-six hours after the onset of tachycardia the pulse returned to normal.

The patient has been symptom free since then.

CASE 3 S K., a 55-year-old Russian merchant, was first seen on November 24, 1940, complaining of pain in the right chest and down the right arm for 5½ months. The physical examination and laboratory examinations were negative except for signs suggestive of atelectasis of the right upper lobe and moderate wasting of the small muscles of the right hand. X-ray examination showed a normal cardiac shadow with a cardiothoracic ratio of 39 per cent and atelectasis of the right upper lobe. Bronchoscopy revealed a mass protruding from the right upper lobe bronchus, subsequently proved to be carcinoma.

On December 13, after a preparatory right pneumothorax, exploratory thoracotomy was performed, which showed mediastinal metastases. Palliative pneumonectomy was done, three 500-cc blood transfusions being given. Except for a transient atelectasis of the left upper lobe that necessitated bronchoscopic aspiration on the 3rd day the course was satisfactory until the 5th postoperative day, when the pulse suddenly rose to 170. Although the patient had no complaints slight sweating was noticed. An electrocardiogram showed auricular flutter fibrillation. Twenty-four grains of digitalis was given in the first 24 hours and $1\frac{1}{2}$ gr daily thereafter. After 20 hours the pulse dropped to 84 but again became rapid after $\frac{1}{2}$ hour. Normal rhythm returned permanently 48 hours after onset. An electrocardiogram was normal except for slightly lowered amplitude of the QRS complexes. One week later, an electrocardiogram showed wide, slurred QRS complexes with depressed ST segments in all leads. The PR interval was 0.13 second. The digitalis was discontinued, and subsequently the ST segments and QRS waves were returned to normal. The patient was discharged symptom free 47 days after operation.

Three months later an electrocardiogram was normal. Death from metastatic carcinoma occurred 11 months after discharge.

CASE 4 C Y., a 66-year-old Chinese bricklayer, was admitted on January 11, 1941, complaining of cough for 5 years and occasional hemoptysis for 2 years.

Physical examination was negative except for dullness and diminished breath sounds anteriorly and posteriorly over the lower half of the right lung and a few crepitant rales at the right base. The usual laboratory findings were negative except that the blood Hinton test was

repeatedly positive. The electrocardiogram was essentially normal. X-ray examination showed a shadow suggestive of atelectasis of the right upper lobe. The cardiac shadow was of normal size and the cardiothoracic ratio was 43 per cent. Bronchoscopy and biopsy showed epidermoid carcinoma in the right lower lobe bronchus.

Following pneumothorax an exploratory thoracotomy revealed that the mediastinum was invaded by the growth. A palliative right middle and lower lobectomy was performed during which two 500-cc blood transfusions were given. On the 2nd postoperative day the pulse suddenly rose to 190 and became irregular. The electrocardiogram showed auricular fibrillation. Fifteen grains of digitalis was given in the first 12 hours, $16\frac{1}{2}$ gr in the first 24 hours, and $1\frac{1}{2}$ gr daily thereafter. Normal cardiac rhythm returned after 48 hours. There were no further cardiac symptoms.

The patient died of metastatic carcinoma 6 months after operation.

CASE 5 N W., a 55-year-old retired manufacturer, was admitted on January 23, 1941, complaining of a slight cough for $1\frac{1}{2}$ years and occasional vomiting for 1 year. He had lost 45 pounds. He took large quantities of alcohol.

Physical examination was negative except for a blood pressure of 160/88, a few crackling rales in the left midchest posteriorly and transient moist rales at the right base. The usual laboratory tests were negative except for a red cell count of 3,540,000, many red cells in the urine and a urinary albumin of 0.1 per cent. A diagnosis of idiopathic hematoma was made after thorough study, including intravenous and retrograde pyelograms. An electrocardiogram was within normal limits except for evidence of slight right axis deviation. X-ray study showed a normal cardiac shadow, with a cardiothoracic ratio of 40 per cent and an infiltration in the region of the left hilum suggesting neoplasm.

On February 3, after a preliminary left pneumothorax a one-stage left pneumonectomy was carried out, three 500-cc blood transfusions being given. The left vagus nerve was found imbedded in the tumor mass and was resected. Convalescence was satisfactory until the 3rd postoperative day, when the pulse suddenly rose to 165 and became irregular. An electrocardiogram showed auricular fibrillation. Twenty-four grains of digitalis was given in the first 24 hours and $1\frac{1}{2}$ gr daily thereafter. Normal rhythm confirmed by electrocardiogram, returned after 48 hours.

The patient was well when examined in January, 1942. An electrocardiogram at that time was normal except for evidence of slight left axis deviation.

CASE 6 R R., a 34-year-old clerk, entered the hospital January 28, 1941, complaining of an intermittent cough for 6 years. In 1937, bronchoscopy and biopsy had shown a benign adenoma in the left main stem bronchus. Deep x-ray treatments and intrabronchial radon were given. The cough and sputum decreased but slight occasional hemoptysis continued. There had been dyspnea on exertion for several years but no edema, orthopnea or palpitation had been present.

Physical examination was negative except that the left chest was limited in motion and there were dullness, harsh breath sounds and many rales over the lower half of the left lung field. The usual laboratory findings were negative. The Decholin circulation times from arm to tongue were 150 and 144 seconds. Other circulation

times from arm to lung were 7.8 and 6.0 seconds. The venous pressure was 86 mm. of water. The vital capacity was 2380 cc. A preoperative electrocardiogram was normal. X-ray study showed atelectasis of the left lower lobe and a large emphysematous cyst of the left upper lobe. The mediastinum was deviated to the left. The exact cardiac thoracic ratio could not be obtained owing to marked displacement, but the heart appeared to be of normal size. Bronchoscopy and bronchography showed marked saccular bronchiectasis of the entire left lung.

On February 11, a left pneumonectomy, with four 500-cc. blood transfusions, was carried out. The course was satisfactory until the 19th postoperative day, when the patient developed a sharp substernal pain not related to respiration. The temperature rose to 102°F. every afternoon and a moderately loud pericardial friction rub appeared. For the next 9 days the patient became progressively worse. The liver increased in size and became tender. An electrocardiogram showed low QRS complexes and low T waves. The venous pressure rose to 200 mm. of saline solution on the 27th postoperative day. A diagnosis of pericarditis with effusion was made, and on March 11, the 28th postoperative day, the pericardium was explored and found to be approximately 0.5 cm. in thickness and shaggy. A loculated collection of approximately 100 cc. of clear fluid was found. The culture was sterile. The following evening the pulse was 170 but regular. An electrocardiogram showed auricular flutter. Twenty-four grains of digitalis was given in the first 24 hours and 1½ gr. daily thereafter. Normal rhythm, confirmed by electrocardiogram, returned in 30 hours. The liver size returned to normal, the abdominal discomfort disappeared, and there was no more chest pain. Improvement was steady. The patient was discharged on August 22.

There had been no more cardiac symptoms when the patient was examined 1 year later.

CASE 7. J. B., a 49-year-old clerk, was admitted on June 15, 1941, complaining of cough and soreness of the right chest for 7 months and blood-streaked sputum for 5 months. A bronchoscopic examination and biopsy on May 23 had shown epidermoid carcinoma of the right main-stem bronchus.

Physical examination was negative except for slightly impaired resonance over the right apex above the level of the 3rd rib anteriorly. The usual laboratory tests were normal. The Decholin circulation time from left arm to tongue was 19 seconds. A preoperative electrocardiogram was normal with the exception of R_4 , which was only 1 mm. high. The cardiothoracic ratio at x-ray examination was 44 per cent.

On June 19, following a preliminary pneumothorax, a one-stage right pneumonectomy, with three 500-cc. blood transfusions, was done. The course was satisfactory until the 3rd postoperative day, when a rapid, irregular pulse was first noticed. An electrocardiogram showed auricular fibrillation with a ventricular rate of 160. Less than 2 hours later normal rhythm spontaneously returned. An electrocardiogram was normal, R_4 being 4 mm. high. The pulse remained regular and between 84 and 98 until the 6th postoperative day, when the patient was awakened by a "fluttering" in the chest and the pulse rate was found to be rapid and irregular. He was given 3 gr. of quinidine sulfate as a test dose. Thirty minutes later the pulse had returned to a normal rhythm of 86.

When seen 3 months later the patient was free of cardiac symptoms.

CASE 8. A. M., a 48-year-old man, was admitted on April 7, 1942, complaining of cough with occasional blood-streaked sputum of 1 year's duration, with a loss of 10 pounds in weight.

Physical examination was negative except for dullness with absent breath sounds over the left upper lung field. The usual laboratory findings were negative except for a red-cell count of 3,860,000 and a white-cell count of 19,900. X-ray study showed consolidation of the upper third of the left lung. The heart appeared normal. The cardiothoracic ratio was well below 50 per cent but could not be measured accurately. A diagnosis of pulmonary abscess was made.

On April 16, following preliminary left artificial pneumothorax, a total left pneumonectomy was performed, three blood transfusions being given. The left phrenic nerve was intentionally crushed. The course was satisfactory until the 15th postoperative day, when a regular pulse of 186 developed. The patient was unaware of the tachycardia. An electrocardiogram showed auricular flutter with a ventricular rate of 170 and an auricular rate of 340. Sixteen and a half grains of digitalis was given in 24 hours. The pulse at the end of that time was 166. During the next 14 hours he received 6 gr. of digitalis. The flutter lasted for 36 hours. On May 3 an electrocardiogram showed a regular sinus rhythm with a rate of 126. An electrocardiogram on May 5 showed sinus tachycardia, with a rate of 132, and one on May 21 showed sinus rhythm with a rate of 118.

There were no further cardiac symptoms.

CASE 9. A. R., a 32-year-old woman, was admitted on April 6, 1942, with a 6-year history of pulmonary tuberculosis limited to the left lung. She had had extrasystole for many years. On February 19, a left pneumonectomy had been done. The postoperative course was satisfactory and the patient was discharged on March 18. She was readmitted for thoracoplasty.

Physical examination was negative except for the lung findings. The usual laboratory examinations were negative. X-ray study showed a clear right lung but pneumothorax on the left. The cardiothoracic ratio was well below 50 per cent but could not be measured accurately.

On April 8, a left thoracoplasty was performed. The course was satisfactory until the 10th postoperative day (8 weeks after the pneumonectomy), when the patient vomited three times without obvious cause and immediately afterward developed a rapid, irregular pulse of 160 to 170. An electrocardiogram showed auricular fibrillation. One and a half grains of digitalis was given intramuscularly, followed by 7½ gr. orally during the next 10 hours. At that time normal rhythm returned for 1 hour, followed by a return of the rapid and irregular rate for 10 minutes. Thereafter the normal rhythm was permanent. Two days later an electrocardiogram was normal.

DISCUSSION

Attempts have been made to discover the cause or precipitating factors that initiate these arrhythmias. The fact that arrhythmia occurred in 8 of 78 cases following pneumonectomy, an incidence of nearly 10 per cent, whereas none occurred in 63 cases following single lobectomy, suggests that the more extensive procedure is essential

to its production. With total pneumonectomy there has been a decided shift in the mediastinum away from the affected side, and later in every case a pleural effusion has developed that required frequent thoracostomy. Although difficult to prove, this shift in the mediastinum may play a part in initiating these abnormal rhythms.

Following closure of the bronchus with silk mattress sutures after pneumonectomy, the vagus nerve on that side naturally falls in close apposition to the closed bronchus, if not actually in contact with it. Therefore infection of the bronchial stump or a stitch abscess in this area would be apt to irritate the vagus nerve. One indication of such an infection may be a rise in temperature. The case records were examined with this in view, and it was found that 2 cases showed a moderate rise in fever at the time the arrhythmia began. One of these patients had been afebrile for one week, when the fever rose to 101°F. without detectable cause. On the third day of fever the arrhythmia began. In 4 cases there was a slight but definite rise in temperature on the day of onset of the arrhythmia. Another patient had a continued temperature after operation, and on the seventh day of fever the tachycardia began. In 1 case the arrhythmia began the day after surgery, when fever is normally present, and hence could not be considered from this point of view. Only 1 patient remained afebrile at the time of the arrhythmia. If this hypothesis is correct, it would explain the variable latent period that follows the operation before onset of the arrhythmia, since the time of onset of the stitch abscess may vary. That vagal stimulation may induce fibrillation under certain conditions has been reported by several workers.¹⁷⁻¹⁸

One might consider further that the mediastinal shift acts like thyroxin or the faradic current and represents the E factor of Nahum and Hoff,¹⁶ and that the E factor combines with vagal stimulation, as suggested by these workers, to induce the arrhythmias.

Sulfathiazole powder was introduced into the chest cavity in 5 cases and sulfanilamide powder in 2 cases. No sulfonamide drug was used in 2 cases. Five patients received sulfathiazole orally after operation, whereas 4 received none. All operations were done under intratracheal cyclopropane anes-

thesia. It seems unlikely that any of these drugs were related to the arrhythmia.

SUMMARY AND CONCLUSIONS

Functional cardiac arrhythmias, especially auricular fibrillation and auricular flutter, occurred in 8 of 78 patients who received total pneumonectomy but had no evidence of heart disease. In our opinion, these arrhythmias alone do not indicate heart disease.

It seems best to restore the heart to normal rhythm as soon as practicable, either by rapid digitalization or, in selected cases, by quinidine sulfate, since heart failure may result if an excessively rapid cardiac rate continues over many days.

The etiology of these arrhythmias is unknown. The hypothesis is suggested that the precipitating factor is vagal irritation from a stitch abscess or infection of the bronchial stump in the presence of hyperexcitability of the auricular muscle resulting from marked displacement of the mediastinum.

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CARDIAC ARRHYTHMIAS FOLLOWING THORACIC SURGERY*

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DISTURBANCES in the rate and rhythm of the heart action are occasionally observed in surgical patients during the postoperative period. The frequency of such occurrences is not high, and no pertinent statistics on this subject are to our knowledge available, although several observers^{1, 2} have noted the frequency of arrhythmias during operation. The uncommonly high incidence of cardiac arrhythmias following thoracic surgery has come to our notice during the last two or three years and deserves some comment. Although at times this complication during the postoperative period is of small consequence and quickly rights itself, at other times it is prolonged and difficult to control. Under such circumstances the physician is confronted with a therapeutic problem that, if not corrected, may result in embarrassment of the heart and the circulation.

In the last few years 12 patients (9 of whom had electrocardiograms) presenting a disturbance in cardiac rhythm following thoracic surgery have been observed in the Massachusetts General Hospital. Nine of these were drawn from a series of 43 patients with carcinoma of the lung who underwent lobectomy or pneumonectomy, a proportion of 21 per cent. The remaining 3 cases were drawn from 13 cases in which exploration (3 cases) or resection (10 cases) of carcinoma of the esophagus was performed. A brief account of these 12 cases is given herewith.

CASE REPORTS

CASE 1. B. M., a 47-year-old Jewish salesman, entered the hospital with a history of productive cough for 7 months, which had been severer for 1 month. For 1 week he had had an intermittent fever as high as 103°F. Physical examination was not remarkable. X-ray examination of the chest revealed an area of increased density that was thought to be due to an abscess of the right lower lobe. On October 14, a right lower lobectomy was performed. Two days later, following the patient's turning on his side and coughing, the pulse became totally irregular at 150 and the lips became somewhat cyanotic. The patient was digitalized in the course of 24 hours, by which time the heart had returned to a normal rhythm. He did poorly, however, and died of infection on October 19, 5 days postoperatively. No autopsy was performed.

Comment. This case illustrates the somewhat transient arrhythmia that may be precipitated by a change of posture. The auricular fibrillation lasted for less than 24 hours.

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CASE 2. F. H., a 65-year-old salesman, entered the hospital with the complaints of wheezing, hemoptysis and some shortness of breath for 8 months. Physical examination revealed a few musical rales throughout the chest. The heart was normal. The blood pressure was 130/80. An x-ray film of the chest demonstrated a mass in the left upper lobe that was thought to be a bronchiogenic carcinoma. On October 25, a left pneumonectomy was performed. The blood pressure dropped postoperatively but returned to normal after 1 liter of air under positive pressure was removed from the left chest. Two days later, the pulse was found to be irregular because of frequent auricular premature beats by electrocardiogram, at a rate of 120. The patient was digitalized, since at first the arrhythmia was thought to have been due to auricular fibrillation. Five days postoperatively, auricular flutter was observed with an auricular rate of 360 and a ventric-

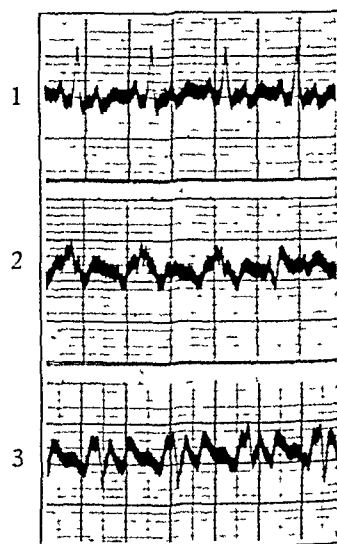


FIGURE 1. Case 2.

The electrocardiogram shows auricular flutter with 2:1 auriculoventricular block.

ular rate of 180 with 2:1 block (Fig. 1). The dosage of digitalis was increased, and the following day the ventricular rate was 120 and there were varying degrees of block. Three days later, a normal rhythm at 100 to 120 with auricular premature beats was observed. The following day auricular flutter was again noted, with a ventricular rate of 160 (2:1 block), and the digitalis dosage was again increased. Two days later, the rhythm was regular at a rate of 120. Later the same day the patient became increasingly dyspneic and cyanotic and died of respiratory distress with the pulse remaining at about 120.

Autopsy revealed the following conditions: epidermoid carcinoma of the left lung (previous operation) with metastases to the liver, kidney and right lung; acute postoperative pleuritis, on the left; acute fibrinous pericarditis; bronchopneumonia; and pulmonary edema and emphysema, on the right.

Comment In spite of the intermittent arrhythmia, there were few signs of heart failure until the last few hours of life. The use of digitalis may have accounted, in part at least, for the lack of more evidence of congestive heart failure. In reviewing the case, however, it appears that quinidine might have been used to great advantage to prevent or control the cardiac arrhythmia. The frequent auricular premature beats in the first electrocardiogram were a sign of an irritable heart.

CASE 3 R. B., a 41 year-old laborer, entered the hospital complaining of chest pain and wheezing of 6 weeks duration. Physical examination revealed a moderate number of musical rales throughout the chest, with some impairment of breath sounds over the right chest anteriorly. The heart was normal. The blood pressure was 100/60. An x-ray film of the chest revealed a mass at the right lung root that seemed to occlude partially the bronchus to the right upper lobe. On May 2, a right pneumonectomy was performed. The patient did well except for the development of moderate subcutaneous emphysema. On May 13, a tube was inserted in the right thorax for drainage of fluid from an empyema. On May 20, the pulse was found to be totally irregular with an apical rate of 135 and a radial pulse of 90. This, however, was readily converted to a normal rhythm in 3 or 4 minutes when the intrathoracic pressure was changed from negative to positive (-5 cm. of water to +2 cm.). No recurrence of the arrhythmia was noted, and the patient recovered from the operation.

Comment The cardiac arrhythmia was of small moment, in this case, but it demonstrates a factor that may influence the cardiac rhythm, that is, a change in intrathoracic pressure on one side of the chest. Change in the position of the heart may have resulted from the change of pressure.

CASE 4 K. B., a 57 year-old physician entered the hospital for observation because of a mass found incidentally by x-ray in the right lung field. The chest and heart were normal. The blood pressure was 110/70. On April 14, a right upper lobectomy was performed for carcinoma of the lung. The postoperative course was uneventful, although the patient was kept in an oxygen tent. On April 14, after he had been out of the tent for a short while, the pulse reached 160, with some irregularity but without deficit. An electrocardiogram revealed the presence of auricular flutter. The patient was digitalized, and the following day the heart rate had decreased to an average of 90, with varying degrees of heart block, from 2:1 to 5:1. Digitalis was continued and the heart rate was fairly well controlled, in spite of the persistence of the auricular flutter, although at times the rate rose to 120. The patient had a slow convalescence with some cyanosis, mental confusion at times and a high carbon-dioxide blood level, which was apparently due to a poor gaseous exchange in the lungs. In July, quinidine sulfate, 0.4 gm. every two hours for six doses, was given in an attempt to restore normal rhythm, but without success. Auricular flutter persisted without acting as a factor of clinical moment until death from cerebral metastatic malignancy occurred the following November.

Comment This case illustrates the long and protracted digitalis was of aid in controlling the ventricular rate.

CASE 5 H. L., a 55 year-old merchant, entered the hospital complaining of cough and hemoptysis of 5 months' duration. The heart was normal and the blood pressure was 140/70. X-ray examination of the chest revealed a mass in the right upper lung field, thought to be carcinoma. The electrocardiogram revealed a normal tracing except for an inverted T wave in Lead 4, which was interpreted as being consistent with mild coronary heart disease. Because of a slightly painful right calf with mild swelling of the leg on entry, the right superficial femoral vein was ligated on February 13. On February 24, a right upper lobectomy was performed. Auricular fibril-

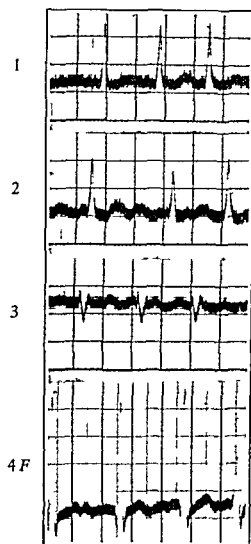


FIGURE 2 Case 5

This electrocardiogram, taken four days postoperatively, demonstrates auricular fibrillation with a ventricular rate of about 145.

lation was noted February 28 (Fig. 2), at which time some fluid was noted in the right chest and the trachea was deviated to the right. Quinidine sulfate was given, 0.4 gm. the first day and 0.8 gm. the 2nd day, at which time the rhythm returned to normal. Following this for 4 weeks 0.2 gm. of quinidine was given three times a day as a prophylactic measure. On March 5, the patient was suddenly seized with a painful constricting sensation across the chest, with increase in the respiration to 35 and in the pulse to 140, with regular rhythm. On the following day, the electrocardiogram (Fig. 3) was quite characteristic of pulmonary embolism with acute cor pulmonale. The same day, tenderness was noted in the left calf, and ligation of the left superficial femoral vein was performed, with removal of a thrombus from the vein. The patient subsequently improved rapidly without further complications.

Comment. It seems likely that quinidine aided in the restoration of normal rhythm. This case also illustrates the occurrence of constricting chest pain quite typical of angina pectoris following a large pulmonary embolism, probably due to decreased coronary blood flow. This is

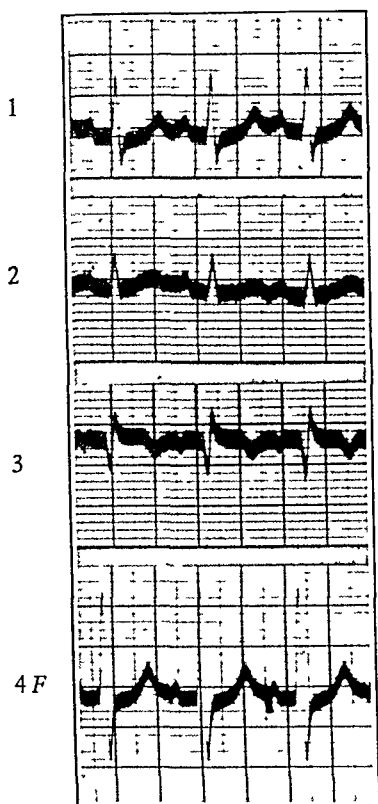


FIGURE 3. Case 5.

This electrocardiogram was taken nine days post-operatively but less than twenty-four hours following pulmonary embolism.

more likely to occur in a patient who has some antecedent coronary heart disease, as was suggested in this case by the slightly abnormal electrocardiogram. It is also of interest that the patient did not develop auricular fibrillation following pulmonary embolism. The maintenance dose of quinidine may have been of some value in this regard.

CASE 6. E. R., a 56-year-old truck driver, entered the hospital because of morning cough and loss of weight for 6 months. The heart was normal. The blood pressure was 130/70. X-ray examination of the chest revealed a mass in the left upper lung field that was thought to be due to carcinoma. On July 6, a total left pneumonectomy was performed. The course was uneventful until July 9, when auricular fibrillation was noted at a rate of 120. The patient was digitalized, and the heart rate was thereafter controlled. He developed fever on July 20, and died from infection on July 22.

Autopsy revealed the following conditions: epidermoid carcinoma of the left lung, with metastases to the regional lymph nodes and contralateral lung; bronchopleural fistula, on the left; septicemia, nonhemolytic streptococcus; and bronchopneumonia (right lower lobe).

CASE 7. J. G., a 57-year-old salesman, entered the hospital with a diagnosis of probable carcinoma of the left bronchus. Physical examination revealed diminished breath sounds over the left lower lobe. The remainder of the examination was not remarkable. The blood pressure was 120/80, and the pulse was regular. On May 22, left pneumonectomy was performed. On May 24, auricular fibrillation was noted, with an apical rate of 110. The patient was given digitalis, 0.3 gm. daily for 7 days, at the end of which time the apical pulse had decreased to 88. Digitalis, 0.1 gm. daily, was continued until discharge. It is not known whether the rhythm was irregular at discharge, but the rate was 80.

Comment. The auricular fibrillation in this case was of little importance and presented no therapeutic problem during the postoperative course.

CASE 8. W. K., a 56-year-old plumber, was referred to the hospital with a diagnosis of carcinoma of the upper lobe of the right lung. Physical examination was not remarkable, and the blood pressure was 120/80. On May 10, a right total pneumonectomy was performed. Three days later, the heart rate was 160, and an electrocardiogram demonstrated auricular flutter at a rate of 320, with 2 auriculoventricular block. Eight tenths of a gram of digitalis was given in the subsequent 24 hours, at the end of which time a second electrocardiogram revealed a normal rhythm at 120 with frequent auricular premature beats. A brief recurrence of the rapid heart action shown to be auricular flutter with a ventricular rate of 160 was observed both on May 11 and May 12, each lasting about an hour. There were no more episodes of disturbed heart action, and the remainder of the course was uneventful. Digitalis was stopped on May 16.

Comment. Again, the transient nature of the tachycardia is demonstrated. It should be noted, however, that evidence of irritability of the heart was manifested at times, in the absence of auricular flutter, by the frequent auricular premature contractions.

CASE 9. J. McC., a 39-year-old mechanic, was referred to the hospital with a diagnosis of carcinoma of the lung. Physical examination was not remarkable, the heart was normal, and the blood pressure was 110/70. On May 10, a right pneumonectomy was performed. On May 11, auricular fibrillation was noted, with a ventricular rate about 190, and this continued until June 2, when the heart rate was regular at 80 with an occasional extrasystole. Later the same day auricular fibrillation was again noted with a ventricular rate of 195. The patient was digitalized which resulted in a decrease of the ventricular rate to 130. The following day 700 cc. of fluid was removed from the right chest. By June 4, the heart rhythm was again normal at a rate of 80 and remained so throughout the postoperative period. Digitalis was continued until discharge.

Comment. The transient nature of the auricular fibrillation is again notable. The accumulation of fluid in the right chest developed about the same time as the auricular fibrillation.

CASE 10. C. H., a 61-year-old laborer, entered the hospital complaining of difficulty in swallowing of 3 weeks' duration. Physical examination was not remarkable. The blood pressure was 155/90. X-ray examination of the esophagus revealed an irregular filling defect in the upper

dle third that was thought to be carcinoma. On July 15 a partial esophagectomy was performed through the left thorax. The postoperative course was uneventful until July 20, when the respirations increased to 30, the pulse rose to 135, and there were physical signs of collapse of the left lower lung. On July 22, the patient became mentally confused and the heart rate was found to be 180. He was digitalized, and the following day the heart rate was regular at 140. The signs of collapse of the left lower lung lobe had disappeared by July 25, at which time the pulse was regular at 95 and the mental confusion had disappeared. Convalescence was uneventful.

Comment. The postoperative period was first complicated by collapse of the left lower lobe, to be followed by the development of auricular flutter and a rapid ventricular rate. Digitalis probably helped to slow the rate and after 3 days normal rhythm was re-established.

CASE 11. C W, a 53-year-old man, was admitted to the hospital because of epigastric pain of 5 weeks duration. The heart and lungs were normal. The blood pressure was 140/70. X-ray examination of the esophagus revealed a tumor in the lower third. On August 3, partial esophagectomy was performed through a left thoracic approach. On August 5 auricular fibrillation was noted with a ventricular rate of 180. The patient was digitalized and 3 days later the apical rate was 100 with normal rhythm. The digitalis was discontinued after 7 weeks, and the heart rhythm remained regular. Convalescence was uneventful.

CASE 12. J L, a 49-year-old housewife entered the hospital because of dysphagia of 7 months duration. Physical examination was not remarkable. The blood pressure was 130/80. X-ray examination of the esophagus revealed an ulcerative lesion in the lower third. On September 7 a transthoracic partial esophagectomy was performed. On October 3 auricular fibrillation developed with a ventricular rate of 200. Quinidine sulfate was started and 7.8 gm was given in the first 24 hours. At the end of this time the rhythm returned to normal for 1 hour at a rate of 110, following which auricular fibrillation recurred with a somewhat slower ventricular rate of 140 to 160. The quinidine was continued the patient receiving 2.8 gm during the 2nd day, in 0.4 gm doses. On October 6 the pulse returned to normal and it remained regular thereafter. The following day 1500 cc of fluid was removed from the left chest. Convalescence was uneventful.

DISCUSSION

Of the 12 patients reported here, 8 developed auricular fibrillation and 4 developed auricular flutter. In 2 cases auricular premature beats were noted either preceding or subsequent to the tachycardia. In no case was there noted a change from auricular flutter to auricular fibrillation or vice versa, but in 4 cases there was at least one recurrence of the arrhythmia following a restoration of normal rhythm. Thus quinidine therapy seems to be justified if auricular premature beats develop or even following the restoration of normal rhythm to prevent any further arrhythmia. It can also be used as a prophylactic measure, particularly in patients who undergo partial esophagec-

tomy, since 3 of 10 patients in our experience developed cardiac arrhythmia. Quinidine sulfate, 0.2 gm three or four times a day, has proved effective in this regard. This need not be given until after the operation, since the arrhythmia does not develop until from two to eighteen days postoperatively.

It is undoubtedly significant that all the patients reported here were thirty-nine years of age or over, the average being fifty-three and range from thirty-nine to sixty-five. In a considerably larger series of patients who underwent lobectomy or, less frequently, pneumonectomy for bronchiectasis of the lung, no cases of arrhythmia of the heart were observed. The ages in that series were much lower, ranging from about fifteen to forty years. Age, then, is a predisposing factor in the development of cardiac arrhythmias following thoracic surgery. This has been noted likewise in patients with otherwise normal hearts in whom a cardiac arrhythmia develops.¹⁻³

In the series of 12 cases reported here, examination of the heart gave no evidence of valvular disease. In 1 patient (Case 5) there was some electrocardiographic evidence of coronary heart disease. However, it has been noted by several observers¹⁻³ that there seems to be no significant association of auricular fibrillation and coronary heart disease. It seems likely, therefore, that coronary heart disease played no important role in the development of the cardiac arrhythmias in this series. It is true that all the patients had carcinoma, but this is undoubtedly irrelevant.

The cause of the development of the arrhythmias remains obscure although there seemed to be precipitating factors in several cases. In 3 cases the development of empyema coincided with the onset of the arrhythmia of the heart, and in 1 there was significant collapse of the lung that developed concomitantly. The change of posture of 1 patient seemed to have initiated the cardiac arrhythmia. Pericarditis was found at necropsy in 1 case, but it seems unlikely that pericarditis was an important etiologic factor in this series.

In treating the patient who develops an arrhythmia the physician has the choice of giving no special treatment, since most of these patients spontaneously reestablish normal rhythm in the course of two or three days of attempting to control the ventricular rate by the use of digitalis and waiting for the normal rhythm to return or of attempting to hasten the restoration of normal rhythm by quinidine sulfate. The decision should be based on the condition of the patient, since immediate therapy may be necessary to avert congestive heart failure. Rapid digitalization is then indicated. If there is no imminent danger of

congestive heart failure, a course of quinidine sulfate, 0.4 gm. every two to three hours for six doses, or until normal rhythm is restored, is the treatment of choice. If this fails, the same course may be repeated, using 0.6 gm. every two to three hours under careful electrocardiographic control.

SUMMARY AND CONCLUSIONS

Cardiac arrhythmia is occasionally noted following thoracic surgery. Twelve patients are reported from a series of 56 who underwent surgery for carcinoma of the lung or esophagus. Eight had auricular fibrillation, and 4 auricular flutter.

Age appears to be a predisposing factor, since arrhythmia of the heart seldom occurs following thoracic surgery below the age of forty.

Quinidine sulfate may be used to advantage in such patients as a prophylactic measure during the postoperative period.

Since the above report was compiled, a thirty-year-old woman has been observed who developed nodal tachycardia at a rate of 180 fifteen hours after a left lower lo-

nectomy for tuberculosis and bronchiectasis. A course of quinidine sulfate, 0.4 gm. every two hours for five doses, was given during the first day without effect on the tachycardia. The patient was also digitalized during this time by the administration of 1.6 mg. of lanatoside C intravenously. A second course of quinidine was given, consisting of 0.6 gm. every two hours, and after the fourth dose, thirty-six hours after the onset of the tachycardia, the rhythm returned to normal and the pulse dropped to 110. Quinidine sulfate, 0.4 gm., was continued every six hours in an effort to prevent the recurrence of the paroxysmal tachycardia. The patient developed increasing cyanosis and died of infection on the fourth postoperative day. The pulse rate remained between 110 and 120 until the time of death.

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MEDICAL PROGRESS

BRIGHT'S DISEASES*

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DESPITE considerable elaboration since the original description by Bright more than one hundred years ago, the group of nephropathies now embraced by the term "Bright's diseases" continues to pose many problems in etiology, pathologic physiology and therapy. In discussing this group of renal disorders, usually defined as the bilateral nonsuppurative nephropathies, a logical classification is desirable. The threefold classification of Volhard and Fahr¹ continues to be popular, either in its original form or in various modifications. Volhard and Fahr's division of Bright's diseases into the inflammatory nonsuppurative nephropathies (nephritides), the degenerative nephropathies (nephroses) and the vascular nephropathies (nephroscleroses) has had a new modification during the past year by Ellis²⁻⁴ in England. He also proposes three groups of entities—nephritis, essential hypertension and a miscellaneous

group. The present review will follow, in the main, the classification of Volhard and Fahr, but will be confined to a discussion of the nephritides and the nephroses. The omission of the nephroscleroses is dictated by the desire to avoid repetition, for this subject is usually discussed with essential hypertension and should be considered in relation to all aspects of hypertension.

THE NEPHRITIDES

Glomerulonephritis

The pathogenesis of glomerulonephritis remains obscure. A considerable amount of work has incriminated the streptococcus as the commonest etiologic agent, although other infectious agents have been implicated as causative factors in isolated cases. There seems to be little doubt that upper respiratory infections, usually by beta-hemolytic streptococci, precede the attack of acute diffuse glomerulonephritis in the vast majority (90 per cent in one series⁵) of cases in this country. It is interesting to note the comment made by Snapper⁶ that a superficial pyodermitis is the usual form of infection preceding acute diffuse

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glomerulonephritis in China. However, Seegal and Earle⁷ found that approximately two thirds of their patients with glomerulonephritis had a "deep" infection. Additional evidence incriminating the streptococcus in most cases of nephritis is to be found in changes in the antistreptolysin titer during the disease, with an increased titer appearing in the acute stage.⁸ During the past year it has also been found that the titer increases in the course of exacerbations of chronic diffuse glomerulonephritis and that the magnitude of the increase is correlated with the severity of the exacerbation and not with the severity of the preceding infection.⁹⁻¹⁰ The increase in antistreptolysin titer is often valuable in detecting a recent infection by Group A hemolytic streptococci, although the organisms may not be demonstrable by culture.

Just how the streptococcus damages the kidney is unknown, for there is no evidence that it directly invades the kidney or has a nephrotoxic effect. Attempts to produce nephritis in animals with streptococci and their products have been on the whole, inconsistent and unsatisfactory. However, a type of glomerulonephritis closely resembling the human form has been produced in animals by the use of "nephrotoxic" serums and may throw light on the mechanism of damage by the streptococcus. So-called "nephrotoxic nephritis" may be produced in the guinea pig, dog, cat or rabbit by injecting serum from ducks or chickens previously subjected to sensitizing doses of kidney tissue from the same species in which the nephritis is to be induced.¹¹ On the surface, this nephritis appears to be caused by a simple reaction between antigen (the recipient animal's kidney) and antibody (the donor's serum). However, if this were the case, the reaction would be expected to occur immediately instead of after five to eight days, as actually found. Moreover, the development of nephritis seems to depend on the presence in the recipient's blood of antibodies reacting with the donor's serum. These antibodies are manufactured during the latent period, and their appearance in the blood marks the onset of nephritis. Kay¹¹ has shown that suppressing the production of these antibodies by roentgen radiation prevents the nephritis, whereas after radiation the injection of antibodies from another animal results in an immediate onset of nephritis. Thus it appears that the first antigen antibody reaction is harmless, but when antibodies to foreign serum are present, a complex is formed that is nephrotoxic. The sequence of events in this type of nephrotoxic nephritis is similar to that in human nephritis, in which a latent period of three to twenty eight days

elapses following the initial infection before the acute episode is manifest, and is consistent with the concept of the causation of human nephritis advanced by Schwentker and Comploier¹² in 1939. In their view streptococcal products unite with the human kidney tissue to form a compound harmless in itself but causing antibody formation. The combination of the new antibodies and the original antibody antigen complex is nephrotoxic.

Studies of the course of glomerulonephritis require many years of careful, tedious and arduous work to come to fruition because of the duration of the disease and the vagaries of its course. During the past year several reports have appeared dealing with the finding of various groups of workers in this field. Ellis²⁻⁴ devoted his Croonian Lectures to a discussion of the natural history of Bright's disease, the result of twenty years' work. He states that glomerulonephritis appears in two forms, which he designates simply as "nephritis I" and "nephritis II". Nephritis I is the commoner of the two forms and appears predominantly in the first two decades of life. It is characterized by a sudden onset of the classic acute diffuse glomerulonephritis, usually following an upper respiratory infection. It proceeds in 82 per cent of cases to complete recovery, but in 10 per cent the disorder becomes latent with persistent proteinuria, terminating as a rule many years later in hypertension and renal insufficiency. Ellis is apparently of the opinion that the nephrotic syndrome is never seen in this group of patients, although it becomes the outstanding clinical manifestation in nephritis II. In this type of nephritis, a much smaller group, the onset is insidious, frequently without a history of a preceding infection, and occurs predominantly in persons in the second and third decades of life. Massive edema, hypoalbuminemia and albuminuria are the dominant and diagnostic features, and nearly all cases progress to a fatal termination in hypertension and uremia. Autopsy material is presented to support the claim that nephritis I and nephritis II are not only clinically unlike but are also definite pathologic entities.

Murphy and Peters¹³ have reported a follow up study of 205 cases of acute diffuse glomerulonephritis. Their findings are in agreement with those of the English workers in indicating a more serious prognosis in those patients who display edema after the first week or two of the disease. They emphasize that they find in their cases of acute nephritis a chronicity rate of at least 59 per cent, a figure in striking contrast to the much more favorable reports elsewhere in the literature. In neither their nor Ellis's study were the length and type of course subjected to further analysis, al-

though they agree on the variability and usual length. In this regard Horn, Klemperer and Steinberg¹⁴ have made an interesting contribution, offering evidence to support the notion that the course of chronic diffuse glomerulonephritis may be divided into two phases, one slowly progressive and the other accelerated. This view is based on a clinicopathological study of 49 cases in which the anatomic equivalents of the changes seen in the benign and malignant phases of essential hypertension were found at autopsy. These changes were associated with histories of slow and of rapid progression, respectively. The authors believe that their data support the hypothesis that prolonged hypertension is the factor exciting acceleration.

There is a varying opinion regarding the prognosis of the initial acute phase of glomerulonephritis. In 495 cases brought together from seven reports, Hayman and Martin¹⁵ found a range of 42.5 to 85.4 per cent cured, 17.3 to 32.0 per cent latent and 3.8 to 41.7 per cent going into chronicity. The greatest difficulty in prognosis is encountered during the latent phase into which many patients pass following the acute attack. This phase may be characterized by the complete absence of outright evidence of renal damage and is often mistakenly overlooked, or the patient is labeled as cured. Addis¹⁶ was one of the first to emphasize the importance of this stage and to study it carefully with a technic of exacting urine examinations, including quantitation of the formed elements in the urine. Addis's method of counting the cells and casts in the urinary sediment continues to be a helpful adjunct in evaluating the progression and prognosis of the disease. Its superiority to the routine urinalysis is seen in the figures of Rubin, Rapoport and Waltz.¹⁷ They found that the routine urinalysis returned to normal on the thirty-seventh day on the average, whereas a normal Addis count required an average of one hundred and twenty days. In addition, they found the sedimentation rate to be as reliable a prognostic index as the Addis count. Murphy and Peters¹³ also recommended the sedimentation rate as a measure of the activity of the disease. From a practical standpoint, the technical simplicity of the sedimentation rate seems to recommend it as a valuable aid in following patients in the latent stage of glomerulonephritis.

There seems to be general agreement that rest is of first importance in the treatment of both the acute episode and the chronic form of glomerulonephritis. Murphy and Peters¹³ state that the patient should be kept in bed until all clinical features and every evidence of nephritis have disappeared, or up to a period of four months. Of

their patients, 27 per cent of those discharged with minimal activity became latent, whereas only 14.9 per cent of those discharged with negative urines went on to latency. However, many workers believe that there is no necessity limiting activity so long as hypertension and edema are absent. It is also agreed that dietary restrictions are indicated in the presence of azotemia and edema. In the former, protein should be limited, and in the latter, the restriction of salt and water is necessary. Whether protein should be cut down in the absence of azotemia remains a moot point. There is no clinical evidence that protein has any detrimental effect¹⁸ and much evidence that protein lack can be harmful. On the other hand, protein feeding has been shown to increase the renal damage of experimental nephritis in animals.^{19, 20} Most clinicians attempt to steer a middle course—the restriction of protein to minimal requirement levels.

The proof that localized infection and particularly infections of the upper respiratory passages and paranasal sinuses may give rise to glomerulonephritis has resulted in an earnest search for and eradication of focal infection. There is no evidence that these procedures ameliorate, interrupt or prevent the renal process. Illingsworth,²¹ studying 119 children with chronic diffuse glomerulonephritis, could find no evidence that the course of the disease was altered by tonsillectomy. Nor could he demonstrate that tonsillectomy was of value in prophylaxis, since 20 per cent of a large series of patients had had tonsillectomy at some time before the onset of the acute nephritis. In another series, seen at the Babies' Hospital in New York City, approximately one third had had their tonsils out before onset.²² Although it seems wise to remove tonsils and eliminate foci of infection in certain cases, this should not be done with the hope of affecting the nephritic process.

The effectiveness of chemotherapy in acute infections, particularly in those of streptococcal origin, has aroused the hope that the sulfonamides might prove effective in prophylaxis, in controlling and terminating the acute attack and in preventing exacerbations. This hope has been given some substance during the past year by the work of Williams, Longcope and Janeway.²³ These investigators treated a series of 42 cases of acute nephritis with sulfanilamide, using an untreated group of 108 comparable cases as controls. They concluded that foci of infection cleared up more rapidly, signs of renal damage disappeared more quickly, exacerbations occurred less frequently, the duration of the edema and the hypertension was shorter, and clinical recoveries were more frequent under sulfonamide therapy than in the

control group Although their conclusions seem warranted by the data obtained, they were not able to present persuasive evidence on every point mainly because of the irregularity of the course of the disease and the relatively small number of cases in their series

Embolie and Other Forms of Glomerulonephritis

Whether the renal lesion appearing in the course of subacute bacterial endocarditis should be included among the nephritides is disputable, although it is widely classified as acute focal embolic glomerulonephritis.²⁴ Christian's^{25, 26} work during the past year seems to support the idea that the lesion is inflammatory, at least in part. He was impressed by the nonspecificity of the glomerular lesions, which resembled those attributable to other glomerular damaging agents, such as acute diffuse glomerulonephritis, pyelonephritis and toxemia of pregnancy. In a series of 61 autopsies he found slight swelling and edema in almost all kidneys, hemorrhages varying from scattered petechiae to the typical "florid" kidney in 13 per cent and areas of infarction in 92 per cent. In 80 per cent the lesions were typical of those seen in intracapillary glomerulonephritis with diffuse proliferative intracapillary lesions, whereas in 16 per cent hyaline thickening of the capillary walls was observed. In addition, epithelial crescents were found in 36 per cent, with evidence of damage to the tubular tissue ranging from focal fibrous lesions in 26 per cent to complete disorganization in a few.

Other conditions in which acute diffuse glomerulonephritis is frequently seen are the visceral angitides, including periarteritis nodosa, lupus erythematosus and Libman-Sacks disease. A study by Krupp²⁷ of the urinary findings in 21 cases of these disorders revealed an apparently specific picture in 14 consisting of the concurrence of red cells, red cell casts, oval fat bodies, fatty casts, broad casts and heavy proteinuria. He believes this concurrence to be of diagnostic significance. The concept of Klemperer, Pollack and Baehr²⁸ that lupus erythematosus is a widespread disease of the collagenous connective tissue will undoubtedly inspire extensive investigation. This hypothesis is based entirely on pathological grounds and has as yet found no experimental proof. However, Rich's²⁹⁻³¹ belief that periarteritis nodosa is a manifestation of hyperergy resulting from sensitization to foreign protein or drugs, such as the sulfonamides, appears to rest on firm experimental evidence. The discovery of extensive fresh lesions of periarteritis nodosa in 7 consecutive autopsies on persons dying in the midst of serum sickness or at the height of a sulfonamide reaction as well as the

experimental production of the lesions in rabbits during delayed reaction to foreign serums, gives strong support to his view. The finding of vascular lesions in rabbits following the production of antibodies to foreign serum has an important bearing on nephrotoxic nephritis, for the production of which these antibodies have been found necessary. Further exploration of the possibilities thus disclosed will undoubtedly add to the knowledge of the causation of many of the nephritides.

Pyelonephritis

Pyelonephritis has taken its place as a member of the group of Bright's diseases only during recent years, mainly as a result of the work of Longcope³² and of Weiss and Parker.³³ The recognition that pyelonephritis can cause hypertension, with the terminal picture, clinically and pathologically, of chronic diffuse glomerulonephritis and malignant nephrosclerosis, and the realization that its initial lesion is amenable to modern therapy, has resulted in a voluminous literature. The acceptance of pyelonephritis with contracted kidney as a form of Bright's disease has not yet found its way into the textbooks, but in the current literature it is tacitly or explicitly regarded as such.³⁴ The fact that many cases of the affection are unrecognized in their incipency raises the question of the relation of pyelonephritis to essential hypertension. The weight of the evidence, however, seems to support the belief that the disease is only slightly more frequent among hypertensive than among normotensive persons. Thus, Shure³⁵ in a review of 11,898 autopsies at the Cook County Hospital in Chicago discovered only 290 cases of pyelonephritis, with hypertension in 44.4 per cent as compared with 34.9 per cent in a control group. Among children, only 10 per cent of 79 cases were hypertensive.³⁶ Moreover, pyelonephritis seems to be a relatively rare disease (in Shure's series 2.44 per cent of the autopsies) and since less than half of these were hypertensive it does not seem likely that pyelonephritis is often an occult cause of essential hypertension. Harrison and Bailey³⁷ emphasize the importance and frequency of this condition as a complication of diabetes, since asymptomatic lesions leading to necrotizing pyelonephritis and death may occur in some 20 per cent of diabetic patients. Bowen and Kutzman³⁸ found in even higher percentage of involvement of the urinary tract in diabetic patients (51 of 84 cases), and they re-emphasized the difficulty of diagnosis. Actually the rarity of the lesion may be more apparent than real since it may be unrecognized pathologically because of the terminal resemblance to chronic diffuse glomerulonephritis and nephrosclerosis. A higher incidence might

be found if the pathological criteria of Weiss and Parker³³—an inflammatory reaction in the interstitium, colloid casts in the tubules, periglomerular fibrosis and evidence of infection or inflammation within the tubules—were kept in mind and applied.

An excellent review of the problems and literature of the glomerulonephritides by Matthews³⁹ has appeared during the past year.

THE NEPHROSES

The group of disorders embraced by the nephroses are diverse in etiology and clinical manifestations, unified only by the fact that in all of them the tubular tissue contains lesions ranging from cloudy swelling with deposits of lipoid and hyaline material to profound necrosis. On the whole, they can be divided into two major categories: those in which the tubular lesions are as a rule of minor importance, with the nephrotic syndrome or proteinuria alone dominating the clinical picture, and those in which necrotic lesions of the tubules are outstanding, associated with few, if any, of the features of the nephrotic syndrome.

Among the entities included in the first group are lipoid nephrosis, amyloid disease of the kidney, intercapillary glomerulosclerosis, nephrosis due to deposit of Bence-Jones proteins in the tubules during myelomatosis—and as minor variants the so-called “larval nephroses”—and benign and orthostatic albuminuria. In all these the common denominator is proteinuria of varying degree. The pathogenesis of the proteinuria remains unknown and controversial, but it is widely held that glomerular capillary permeability is the determinant of the quantity of protein appearing in the urine. Dock⁴⁰ has advanced the thesis, on the basis of studies of the behavior of large protein-bound dye molecules, that a considerable amount of protein traverses the glomerular membrane normally and is reabsorbed by the tubules. In his view such entities as benign albuminuria, orthostatic albuminuria and other varieties of moderate protein loss may be attributable to tubular dysfunction rather than to increased permeability of the glomerular capillaries. Nonetheless, in cases of major proteinuria his concept must also embrace the notion of increased glomerular capillary permeability. Dock's hypothesis seems to gain support from the work of Smetana and Johnson.⁴¹ These workers found that the colloidal and lipoidal droplets in the tubule cells of urodeles are derived from reabsorbed protein, a finding that indicates the possibility of protein reabsorption in the mammalian kidney and offers an explanation for some of the pathological findings in the nephrotic syndrome. An extensive study by Blackman, Goodwin and Buell⁴² throws

light on the components of lost protein and the significance of various types of proteinuria. In general it appears that albumin makes up the largest moiety of the protein lost, but in conditions of progressive renal failure associated with the appearance of fibrin and organized exudates within the kidney there is high globulinuria. Fatal cases of acute diffuse glomerulonephritis associated with high proteinuria and globulinuria showed extensive deposits of fibrin within Bowman's capsule, unlike fatal cases in which the proteinuria was of low concentration. However, the loss of protein in the urine, no matter what its mechanism, is the cause of the clinical picture in those conditions where proteinuria becomes excessive, for protein loss in excess of restoration causes hypoproteinemia, a lowered plasma oncotic pressure with subsequent edema, and the full-blown nephrotic syndrome.

The nephrotic syndrome is not limited to the nephroses, for it frequently appears in acute diffuse glomerulonephritis or in the course of chronic diffuse glomerulonephritis. It is interesting that this picture is always associated with an increase in the plasma lipids. The increase in blood lipid is regarded by some as a mechanism by which the lowered oncotic pressure may be compensated. However, Farr, Smadel and Holden⁴³ have shown that hyperlipemia is a constant feature of severe nephritis induced in rats by antikidney serum when there is no hypoproteinemia, and Heymann⁴⁴ reports that lipemia may occur on the basis of tubular damage in the absence of a decreased oncotic pressure. Heymann found a continuous rise in cholesterol and an even greater elevation in total fat following bilateral nephrectomy and fatal renal damage by mercury or uranium, but the levels returned to normal following hypertrophy of the remaining kidney after unilateral nephrectomy or healing of the renal damage. Winkler and his co-workers⁴⁵ also found an elevation in the phospholipids after bilateral nephrectomy and ligation of the ureters, but were unable to obtain increases after unilateral nephrectomy. They showed that the response was nonspecific, occurring in the monkey as well as in the dog, and was not due to fasting, dehydration or reduced plasma volume. An increase in the liver lipids indicated an extrahepatic source, and they expressed the opinion that the hyperlipemia might be due to a disturbance of a renal role in fat metabolism. In addition, Moschowitz⁴⁶ found that hyperlipemia appeared in many conditions in which there was decreased metabolism, and he postulated that the hyperlipemia was caused by the decreased metabolism consequent on generalized edema. Thus there is no evidence that a disturbance of lipid metabolism is of primary im-

portance in lipid nephrosis except as a phenomenon secondary to other changes.

Whether lipid nephrosis is a distinct disease entity dominated clinically by the nephrotic syndrome, pathologically by lipid deposits in the tubular cells and anamnestically by the absence of preceding renal disease, often with a fatal termination in the "nephrotic crisis" (explained below), is not certain. It is quite clear that the picture of lipid nephrosis is extremely rare, for Schwarz, Kohn and Weiner⁴⁷ have seen but 40 cases in a twenty-year period at the Mount Sinai Hospital in New York City, where proportionately more cases are observed than elsewhere because of the intense and long-standing interest in the subject among many workers there. Of these 40 patients, 22 are now dead, of whom 12 were examined post mortem. At autopsy 5 showed definite glomerular changes. One case proved particularly interesting, for an onset of typical acute diffuse glomerulonephritis was followed by a typical clinical picture of lipid nephrosis and death due to pneumococcal peritonitis. At autopsy only an occasional glomerulus with a thickened capsule and swelling of the tuft adjacent to it was found. The authors conclude that most children with the classic clinical picture have glomerular involvement, but perhaps in a different form than that seen in chronic or latent glomerulonephritis. Moschowitz,⁴⁸ a member of the same group, concludes

The validity of "lipid nephrosis" as a distinct disease entity depends on whether it possesses a precise background clinically and morphologically. Clinically "lipid nephrosis" can be differentiated from conditions that simulate it only by arbitrary criteria. Anatomically, "lipid nephrosis" has no specific or consistent background. . . . In the last analysis, "nephrosis" is not a disease and requires precise definition when the term is employed.

In any event, as Farr⁴⁹ has pointed out, the physiologic features and therapeutic implications remain unchanged regardless of the final position of the syndrome nosologically.

Considerable advances have been made during the past few years in knowledge of the physiopathologic phenomena associated with this syndrome. Farr⁴⁹ has recently written an admirable review of these advances, for many of which he and his colleagues are responsible. He is attracted to the idea that the syndrome is not essentially a renal affair. This notion finds support in the finding of a normal kidney function as measured by the urea and inulin clearances and in the evidence of a disturbance of protein metabolism. In both children and adults with the syndrome there is difficulty in maintaining nitrogen equilibrium even on high-protein diets. In addition, there appear to

be abnormalities of the plasma proteins demonstrable immunologically and electrophoretically. Additional evidence that a defect in protein metabolism is responsible for nephrosis is found in the frequent occurrence of what Farr calls the "nephrotic crisis" associated with hypoaminoacidemia. The nephrotic crisis consists of an acute febrile episode with symptoms of peritonitis in the presence or absence of peritoneal infection. Farr and his associates have shown that these episodes are usually preceded by an accelerated loss of urinary nitrogen and a drop in the plasma level of the aminoacids. Intensive treatment with intravenously administered aminoacids or casein hydrolysates has not prevented or halted these episodes but seems definitely to have lessened the fatalities from them. In 32 cases treated with aminoacids, Emerson and Van Slyke⁵⁰ had no deaths, as contrasted with 66 per cent mortality when aminoacids were not used.

(To be concluded)

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**BENJAMIN CASTLEMAN, M.D., *Acting Editor*EDITH E. PARRIS, *Assistant Editor*

CASE 29341

PRESENTATION OF CASE

A thirty-six-year-old white bank clerk entered the hospital because of increasing dyspnea of three months' duration.

The patient had had a long history of respiratory distress. Nineteen years prior to admission, while in college, he had had two attacks of pneumonia within a few months. Tuberculosis was suspected but chest plates failed to confirm the diagnosis. For the next ten or twelve years he was well except for more than the usual number of colds. Seven years before entry he was examined for life insurance; in view of his past history an x-ray film of the chest was taken which showed a lung tumor. He was admitted to an outside hospital where, following artificial pneumothorax, an exploratory thoracotomy was performed. A diagnosis of inoperable malignant tumor of the lung was made. He recovered from the operation and returned to work, free of symptoms.

During the next two years he lost about three months each year from his work because of upper respiratory infections. He was given x-ray treatment every three months. Two years later, that is, three years prior to admission, he had pneumonia again. About one year prior to admission he was told by his physician that they had considered his lung tumor malignant and incurable but that since he had lived for so many years they had become convinced that the tumor was benign. For the following two or three months he developed episodes of palpitation, which he believed were due to "nerves." These passed off and did not return. Three months prior to admission he had the gripe. Following this there was a gradual onset of dyspnea, which prevented him from walking up hill or climbing stairs. Three weeks before entry the dyspnea cleared up for a short time, but soon returned and became progressively worse. There was no history of tuberculosis.

Physical examination showed a thin, pale man with a sallow complexion. There was some in-

creased prominence of the veins of the forehead and neck. The left border of cardiac dullness was 16 cm. to the left of the midline in the seventh interspace. The heart was otherwise normal. The lungs showed dullness over the right apex, becoming flat at about the level of the fourth rib. The entire right lower lung was flat, with absent breath sounds and decreased fremitus. The left lung was resonant, but there were occasional rales at the base. The abdomen was negative except for a tender liver edge, which could be percussed 8 cm. below the costal margin.

The blood pressure was 110 systolic, 90 diastolic. The pulse rate was between 100 and 130, and the respiration between 20 and 25. The temperature was normal.

The hemoglobin was 11.3 gm. per 100 cc., and the white-cell count 13,600. A blood Hinton test was negative. Two sputum examinations were negative for tubercle bacilli.

An x-ray film of the chest showed complete obscuring of the lower two thirds of the right lung field by fluid. The right upper lung showed increased density with honeycombing. A grid film showed the right main bronchus visible for about 2 cm., beyond which it could not be made out. The left lung field was clear. The heart shadow was tremendous, and the configuration suggested pericardial effusion (Fig. 1). Fluoroscopically no pulsation was demonstrable. The mediastinum was not displaced. Repeated x-ray examinations revealed no additional findings. A chest tap in the eighth space in the subscapular region yielded 30 cc. of light-amber fluid, followed by 220 cc. of what appeared to be whole blood. This was removed from several directions and depths. A repeat tap in the seventh space in the midaxilla again yielded 30 cc. of blood. No tumor cells were seen in the fluid, which contained innumerable red cells. Two days later the venous pressure was recorded at 330 mm. of water (normal control, 137 mm.). The patient was refluoroscoped at that time. A definite pulsation of the heart could be seen. No change in the contour of the heart could be demonstrated on changing the position of the patient from erect to horizontal. The left border of the heart shadow was convex and without any break in the smooth curve to indicate the limits of the pulmonary conus and left ventricle. Laminography showed the right main bronchus to end sharply 2 cm. from its bifurcation (Fig. 2). No air could be seen entering the lower and middle lobes. There was narrowing of the upper bronchus extending into the aerated portion of the lung. Several small air-filled areas were seen in the region of the lower lobe. A dense soft-tissue mass was seen lying between these and the

*On leave of absence.

blocked right main bronchus. The outline of the mass could not be clearly defined. An electrocardiogram was interpreted as showing sinus tachycardia, with a rate of 120, slight right-axis deviation, low T_1 , total inversion of CF_2 and a very low T in CF_4 and CF_5 .

The patient's dyspnea increased progressively. He died on the twelfth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. C. SIDNEY BURWELL*: I should like to try to reconstruct some stages of this gentleman's

tion from either the superior or inferior caval areas. We do not have a measurement of the venous pressure on the femoral vein, but there was evidence on physical examination that the liver was greatly enlarged and tender. I should accept that as evidence that he had an elevated pressure in his whole venous system. To that should be added the observation on his pulse pressure, which was very low, — only 20 mm., — with a low systolic and a high diastolic pressure. No statement is made about the presence or absence of paradoxical quality. The patient had an extremely rapid

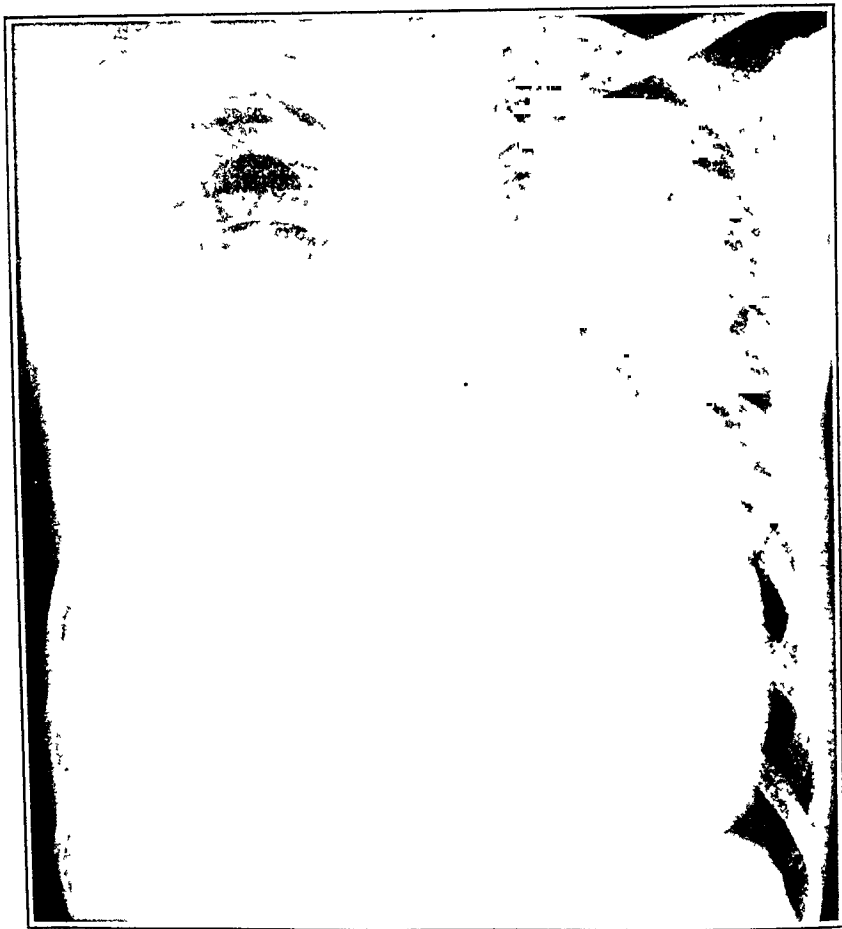


FIGURE 1. *Roentgenogram of the Chest.*

course, beginning at the time he came into the hospital, to see what specific statements we can make that seem reasonably acceptable concerning the anatomic and functional situation of the heart and lungs.

In the first place it seems to me demonstrable that this man had an interference with the entry of blood into his heart—that he had pericardial tamponade. This conclusion is based on the following observations. He had distended neck veins and an elevated venous pressure; there is no mention of the development of collateral circula-

tion without fever, again a characteristic finding in those who suffer from obstruction of the entry of blood into the right side of the heart. This conviction of the presence of cardiac tamponade is strengthened by the observations that seem to indicate that he had a pericardial effusion of considerable size—namely, a very large heart shadow and what could be described as an “expressionless” heart, which neither moved nor exhibited the landmarks on the contour which we are accustomed to recognize. Thus he had a large, nonpulsating, smooth, heart shadow, combined with evidence of obstruction to the entry of blood into the heart, and I think we can say

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that he had pericardial effusion, with obstruction to the flow of blood from the venous system into the heart.

Now let us turn our attention to the pulmonary situation at the time he came into the hospital. That also seems to me to be impressive from the point of view of its mechanics rather than from the point of view of information concerning its etiology. The patient had, quite clearly, a long history of progressive obstruction to the bronchi

series of collapses of the middle and right lower lobes, ending up in the situation in which he entered the hospital. More recently he had probably had beginning obstruction of the upper branch of the right main bronchus, with a similar change in the right upper lobe. Thus I should place pericardial effusion and pericardial tamponade as the first part of our diagnosis, and bronchial obstruction with atelectasis and bronchiectasis as the second.



FIGURE 2. Laminogram Showing Obstruction of the Right Main Bronchus just below the Upper-Lobe Orifice.

of the right lung. I surmise that the course of events was an obstruction to one or the other branch of the right bronchus, leading to atelectasis beyond the point of obstruction and to the development of bronchiectatic cavitation, probably recurrent infections in the atelectatic lung, destruction of lung tissue and the leaving of this honeycombed structure as the late result of bronchial obstruction. It seems to me that that meets the situation better than the possibility—the remote possibility it seems to me—of congenital polycystic disease of the lung. This man, I should say, had had a

Then we come to the most important and difficult part of the discussion—the basis for these mechanical changes in the lung and heart. Are they to be placed fundamentally on an inflammatory disease or on a neoplastic basis? Let us consider the possibility of a unitarian basis—that everything can be explained on one etiologic factor. What about tuberculosis? We know that tuberculosis of the bronchi is commoner than we thought; that enlarged lymph nodes in the mediastinum or the hilus of the lung may invade the bronchi and lead to inflammatory stricture and to

obstruction. Let us consider the possibility that he had reactivation of the mediastinal nodes and invasion of the pericardium by tuberculosis. It seems to me there are at least three very important pieces of evidence against the hypothesis that it had been or was tuberculosis, particularly the latter. One is the fact that he was quite free of fever, and I take it that the observation of a normal temperature was not a single isolated reading at a moment after a cold bath or something of that sort, but did really reflect the situation while he was in the hospital. I see from the chart that he never had fever over 101° F. and that it was usually around 99° . That seems to me strong evidence, not final, against an active pericardial tuberculosis. The second piece of evidence against the possibility of tuberculous pericarditis is the presence of blood in the fluid that was removed presumably from the pleural cavity. It may have been removed from some other cavity in relation to the right lung, since the first tap conceivably might have been into the pericardium; but wherever it came from the fluid was so bloody that it was less characteristic of a tuberculous lesion than of a neoplasm involving either the pleura or the pericardium, or both. There is no particular case for the position, so far as I can find out, that a primarily tuberculous lesion may undergo malignant degeneration and be the site of tumor. Another important argument against the presence of tuberculosis is the observation seven years before entry, when his chest was opened and the surgeon, who had the inestimable advantage of a direct view, saw something he believed to be an inoperable malignant tumor of the lung. It is conceivable that that was on a tuberculous basis, but I think that it is much likelier to have been a neoplasm.

If we set aside tuberculosis, we are then confronted with the necessity of postulating a neoplasm. This is certainly the commonest cause of bronchial obstruction. Assuming it was a tumor, it had the extraordinary dual capacity of existing at least seven years—possibly more—and at the same time having done something recently that sounds very much like malignant invasion of neighboring structures. We must consider various types of benign tumors that obstruct the bronchus,—the adenomas and various other ones,—some of which may undergo malignant degeneration after years of growing. We must consider lymphoma. It does not appear in the record whether or not the x-ray treatment, which was faithfully administered, had any effect. However, if it had had an effect, we probably should have been so informed. I am trying to interpret that evidence, such as it is, as indicating that it was not the type of specific improvement after

x-ray that we should expect if we were dealing with a lymphoma.

There is a curious silence about the state of this man's cough and sputum. I think one must interpret that as indicating that cough and sputum were not remarkable, and I derive from that the suggestion that hemoptysis was not a vigorously presenting symptom.

So we have quite an assignment—a neoplasm that obstructed the bronchus but did not produce much cough, did not produce large amounts of sputum, did not lead to hemoptysis and had lasted all these years, to explode in an extension to the pleural and pericardial cavities. At the time of the onset of his disease, this man was twenty-nine years old, a situation that further narrows the probabilities regarding the nature of the hypothetical neoplastic process. I do not think, by the way that he had an aneurysm. There is no suggestion in his history or in the serologic findings. The patient was too youthful to have had an aneurysm that lasted as long as this, and I do not believe that the blood that came out at the time the chest tap was done was due to the entrance of the needle into an aneurysm.

If we ask ourselves what are the types of neoplasm that might fulfill this order, we certainly should have to consider carefully the small group of tumors arising from the mediastinum—the dermoid cyst, the teratoid tumor and so on. These do occur in men of this age. Most of them make themselves known before thirty or forty. Most of them have announced themselves, if they are going to grow, by the time the patient is forty. They almost always start in the anterior mediastinum and are more apt to go to the right than to the left. They are known to compress and occlude the right main bronchus or its main branches, and they may secondarily undergo late in their development the type of malignant change that it seems to me is suggested by the recent developments in this man's history. But unhappily for me, he never spit up any hair or teeth or had any of the other charming observations that serve to make a positive identification of such a tumor. However, it seems to me that that group—probably a dermoid cyst with malignant change—fits the bill better than any other type of tumor I can think of.

The commonest tumor, of course, to give the kind of termination is bronchiogenic carcinoma. Bronchiogenic carcinoma with an onset at twenty is not impossible, but one that lasts for seven years is certainly an extreme rarity. According to the statistics I could put my fingers on, the great majority of people with bronchiogenic carcinoma do not live for more than five years. In fact the

longest duration that I could find in recorded cases of bronchiogenic carcinoma was between five and six years.

There is one other point. This man had had attacks of palpitation. Whether these were because he was nervous, or because he was anemic, or whether these attacks were associated with paroxysms of tachycardia or fibrillation I do not know. Such paroxysms occur frequently in people with pulmonary or mediastinal carcinoma, or with actual invasion of the pericardium by carcinoma, and the record does suggest that these attacks may have been brought on by such a mechanism.

I shall conclude by saying that I believe this man had a pericardial effusion, pleural effusion and bronchial obstruction with atelectasis, and that this was based on an extramural neoplasm that eventually involved the walls of the bronchi. This tumor was originally benign but eventually underwent malignant change and extended to the pericardium. Of all types of neoplasm, I consider a dermoid cyst to be the likeliest origin.

When one thinks of pericardial obstruction or distention in a case of neoplasm, one has to consider the possibility that it is due not to fluid but to actual invasion of the pericardial cavity by solid tumor. I know only two ways to make the diagnosis: to find cells in the pericardial fluid, which is comforting, or to see a shadow of the pericardium that is not smooth but lumpy. That may be inflammatory, of course, but is likely to be tumor.

DR. BENJAMIN CASTLEMAN: Dr. Sweet, you said that the pericardium was tapped. Is that correct?

DR. RICHARD H. SWEET: Yes. The reason it is not in the record is that I did it myself and forgot to write it down.

I did a pericardial tap through the paraxiphoid region first and obtained fluid readily. But it looked to me to be whole blood, and after drawing off a few hundred cubic centimeters, I withdrew the needle because I did not want to bleed the man to death. At the suggestion of Dr. Conger Williams, who saw this man with me, I then inserted the needle laterally to the first tap and the same kind of fluid was obtained; I could feel the pulsation of the heart muscle with the needle. We were sure that he had a massive effusion. Since the fluid was so much like whole blood and since the patient had a red-cell count of 2,500,000, I desisted. At a later chest tap we also removed whole blood.

DR. BURWELL: If it was fluid blood,—and I think it must have been,—that strengthens the case for rapidly growing neoplastic invasion. The presence of blood in the pericardium is due either to trauma, to cardiac rupture or to neoplasm. The

inflammatory fluid from tuberculosis may contain red cells, but it is not usually grossly bloody.

What about his sputum?

DR. SWEET: The patient never had any hemoptysis. He had a lot of cough and Dr. Burwell was correct in his interpretation of the bouts of what the doctors called variously grippe, pneumonia or what not, which must have been due to bronchial obstruction. After the patient died I obtained a report from the surgeon who operated on him seven years previously. He was convinced that the pulmonary tumor was a carcinoma.

DR. BURWELL: Not a shriveled-up lobe?

DR. SWEET: No; he saw a large round mass.

DR. BURWELL: It was within the right lung?

DR. SWEET: Yes, in the region of the middle lobe. Unfortunately no biopsy specimen was taken.

I never entertained any thought of operating on the patient, but tried to establish a diagnosis. My conclusion was that he had a teratoma.

DR. BURWELL: No teeth could be seen in any of the x-ray films?

DR. SWEET: No; however, I do not mean a dermoid cyst. A teratoma behaves differently from most of the dermoid cysts in the mediastinum that I have seen.

DR. CASTLEMAN: I am sorry that Dr. Conger Williams is not here, but I shall read his note:

I am in favor of the diagnosis of pericardial effusion with tamponade to explain the findings of high venous pressure, paradoxical pulse and large cardiac shadow without evidence of valvular disease or anything to suggest diffuse myocardial involvement. Additional suggestive findings are left-border dullness 2 cm. outside the apparent apex impulse and narrowing of the border of superior cardiac dullness on the left in the sitting position in comparison with the lying position. There is probably some displacement of the heart shadow to the left, but it does not account for the large cardiac shadow. The blood pressure of 108/78 is not especially impressive, but does not exclude the diagnosis. The fact that the heart sounds come through well does not rule out pericardial effusion. Also in favor of pericardial effusion, as against heart failure, is the fact that the patient can lie flat on his right side without dyspnea.

CLINICAL DIAGNOSES

Teratoma of mediastinum, with extension to right bronchus and pericardium.
Pericardial effusion, with cardiac tamponade.

DR. BURWELL'S DIAGNOSES

Malignant dermoid cyst of mediastinum, with extension to right bronchus and pericardium.
Pericardial effusion, with cardiac tamponade.
Pulmonary atelectasis and bronchiectasis.
Pleural effusion.

ANATOMICAL DIAGNOSES

Carcinoma of the lung, with extension to pericardium, right auricle and pulmonary vein and partial obstruction to superior vena cava.

Pericarditis, acute and chronic, with hemorrhagic effusion.

Cardiac tamponade.

Pulmonary atelectasis, with cholesterosis, right middle lobe.

Hydrohemothorax, slight, right.

Pleuritis, chronic, fibrous, right.

ing bronchial obstruction. The middle and lower lobe bronchi were filled with tumor nodules. This tumor had extended medially to involve the right side of the pericardium, and the pericardial cavity contained a liter of bloody fluid. The visceral pericardium was covered with a shaggy brownish-red fibrinous exudate. The tumor apparently had extended through the wall of the parietal pericardium and had bled into the pericardial cavity. There was no actual tumor on the visceral layer, so that all this blood in the pericardial cavity was due to oozing from the tumor the

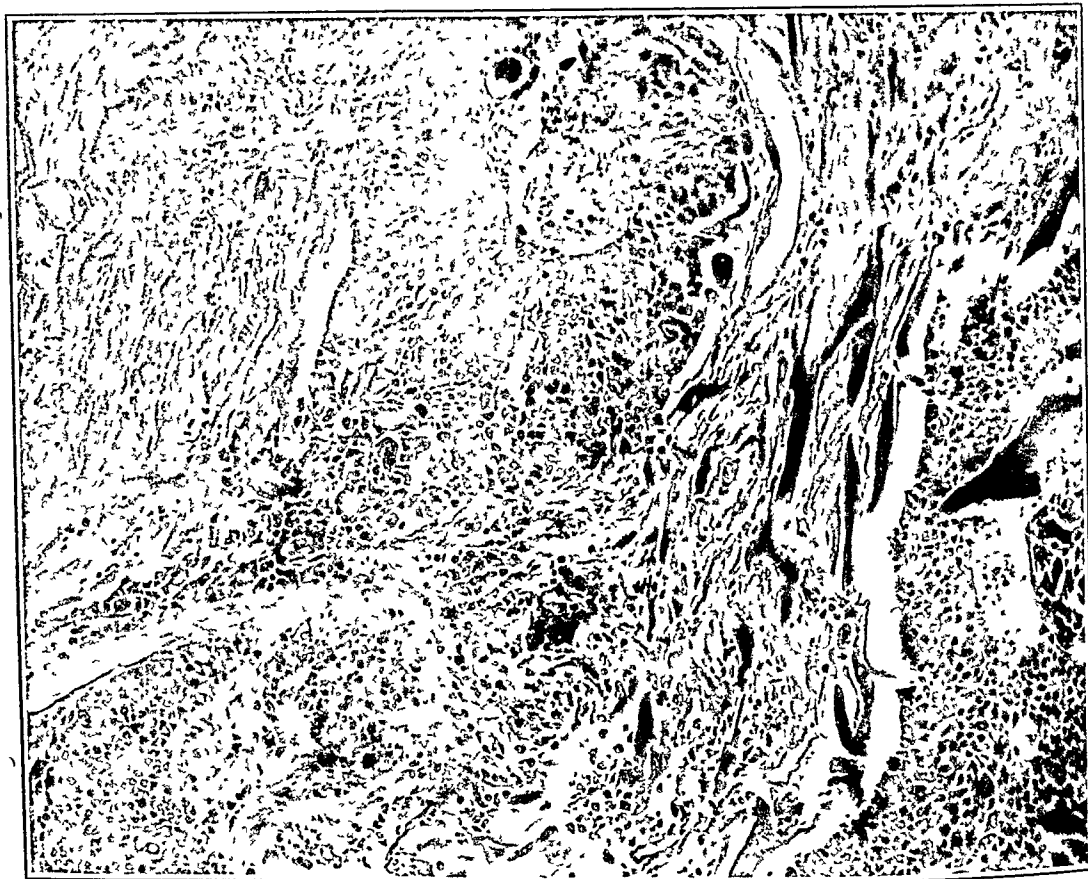


FIGURE 3 Photomicrograph of Tumor Invading the Myocardium of the Right Auricle.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: There was only about 100 cc. of hemorrhagic fluid in the right pleural cavity, but most of the cavity was obliterated by dense fibrous adhesions. Most of the right lung was replaced by a grayish-white granular, soft tumor with many areas of necrosis, one of which formed a cavity measuring about 3 cm. in diameter in the lower lobe. The tumor involved the entire lower lobe and the lower four fifths of the upper lobe. The middle lobe was entirely collapsed and fibrotic and was mottled yellowish orange, owing to the large deposits of cholesterol. This so-called "cholesterosis" of the lung is not uncommon with long-standing

had penetrated through the parietal layer. It also penetrated through the right auricular wall into the auricle, obliterating a large part of the cavity, blocking the orifice of the superior vena cava, but without involving the endocardium. The tumor had also extended from the lung into the lower pulmonary vein for a distance of 4 cm. and had almost reached the left auricle. A photomicrograph (Fig. 3) taken through the right auricular wall shows tumor cells replacing myocardial fibers. The tumor cells are epithelial in character. There is no stroma between the cells and without knowing anything about the disease I am sure every pathologist would call this straightforward carcinoma of the lung. With the in

mation that the tumor was of at least seven years' duration one might be justifiably skeptical of a diagnosis of carcinoma and might then bring up the diagnosis of endothelioma, possibly arising from the pleura.

DR. BURWELL: That would account for the extraordinary bleeding

DR. CASTLEMAN: Most of the tumors of the pleura diagnosed as endothelioma are carcinomas of the lung with extension to the pleura. In fact we rarely if ever make the diagnosis of endothelioma. The cases that have been reported as endothelioma usually have nodules all over the pleura and are associated with a hemorrhagic effusion. There were no nodules on the pleura in this case. Another theory of the origin of this tumor is that it arose from a bronchial adenoma. The right bronchi were filled with tumor, which may have been benign years ago and then became malignant, as a few of them do. We know that adenomas are prone to extend through the bronchial wall and form large extrabronchial tumors. Perhaps the tumor felt seven years ago may have been an adenoma. If that were true, it is strange that the patient had no hemoptysis.

DR. BURWELL: That is what troubled me.

DR. CASTLEMAN: Nevertheless, I think we have to make a positive diagnosis at autopsy of carcinoma of the lung with extension into the pericardial cavity and into the heart. There was a metastasis to an intrapulmonary lymph node, close to the tumor, but no distant metastases.

DR. J. H. MEANS: Would you grade it as a slowly growing malignant tumor because it has been there for seven years? It must have been growing slowly.

DR. CASTLEMAN: It was not rapidly growing, but certainly not slowly growing.

DR. BURWELL: Is that not an extraordinary duration?

DR. MEANS: It does not seem possible that a carcinoma of the lung could have been present for seven years.

DR. CASTLEMAN: I was also puzzled and showed these slides to two other pathologists, who agreed to the diagnosis of carcinoma.

DR. BURWELL: Suppose it had been an adenoma. Might it not have developed deep enough in the mucosa so that it went outward instead of inward?

DR. CASTLEMAN: All the adenomas with extrabronchial extension that we have seen also have a nodule of tumor protruding into the lumen, unless, of course, it had been removed bronchoscopically.

DR. BURWELL: It seems to me evident that whatever this was seven years ago, it was a carcinoma

at autopsy. The problem that has to be settled is the presence of an obstructing lesion seven years previously that eventuated into a carcinoma of the lung.

DR. CASTLEMAN: I believe that one can have a carcinoma of the lung of low-grade malignancy for seven years. A case that Dr. Allen discussed recently was a hepatoma of nine years' duration.* I think the whole idea of long-standing malignant tumors is something that we perhaps do not appreciate sufficiently.

DR. BURWELL: He had no hemoptysis.

DR. SWEET: No, which suggests that the tumor did not arise in a large bronchus.

DR. BURWELL: That is one of the reasons why I thought of an extramural source.

DR. SWEET: I was convinced all along, until I saw the autopsy, of mediastinal origin.

CASE 29342

PRESENTATION OF CASE

A twenty-nine-year-old housewife entered the hospital because of sharp pain in the right hip that radiated down the right leg.

Approximately five months prior to admission, without previous trauma, she developed sharp pain in the right hip that radiated down the right leg to the foot. At first this was mild and sporadic but during the previous four months the pain had occurred daily, had interfered with walking and had often kept her awake at night. On several occasions the right foot felt slightly numb and there were "pins and needles" in the foot. About three months prior to admission the pain became so constant and severe that she did not dare leave the house for fear that she would collapse. Five weeks before entry she fell down three stone steps, landing on her left side. After this her back was constantly sore.

Physical examination disclosed a thin woman who seemed comfortable. She walked with a slight tendency to favor the right leg. The pelvis was held level, but there were moderate lumbar lordosis and slight dorsal kyphosis, and the weight-bearing axis seemed displaced posteriorly. Examination of the heart and lungs was negative. In the right lower quadrant of the abdomen was a 1 by 2 cm. area of pigmentation suggestive of a "café-au-lait spot." There was no tenderness over the spinous processes. There was questionable fullness in the right iliac fossa, and slight tenderness to deep palpation in the right pelvic fossa, but no mass was felt. There was no pain

*Case records of the Massachusetts General Hospital (Case 29331). *New Eng J Med* 226: 347-348, 1943.

on compression of the pelvic brims. Straight leg-raising on the right was limited to 75° because of tightness in the hip. However, there was a full range of hip and knee motion with the leg flexed.

The blood pressure was 95 systolic, 60 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a red-cell

showed slight enlargement. The cortex appeared normal. The remainder of the visible skeleton showed no evidence of decalcification. No abnormal soft-tissue masses were seen. The pelvis was slightly tilted to the left. Films of the right lower femur and of the upper part of the lower right leg showed no evidence of bone pathology. Films of the chest were negative. An

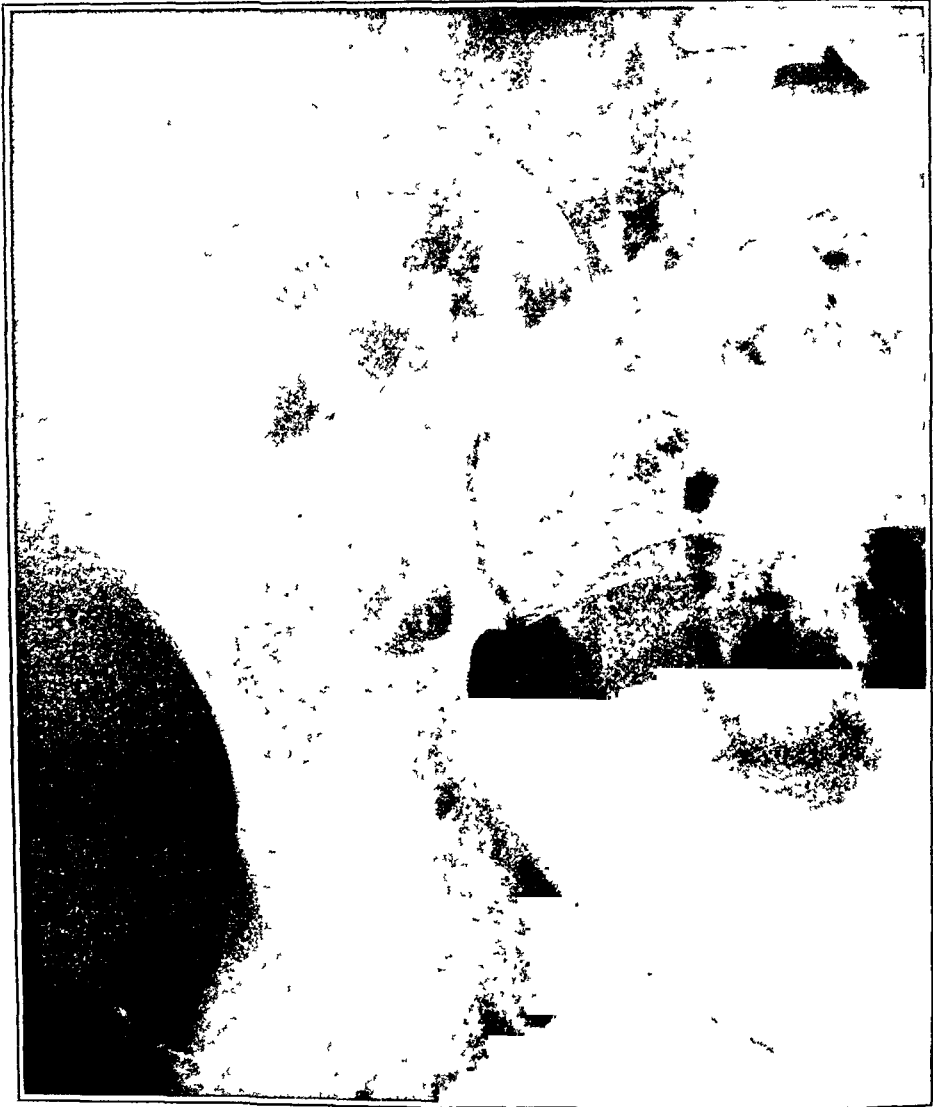


FIGURE 1. *Roentgenogram of the Right Ilium.*

count of 4,280,000, with a hemoglobin of 80 per cent, and a white-cell count of 6300. The urine was negative except for a ++ Sulkowitch test for calcium. A blood Hinton test was negative. The serum calcium was 10.5 mg.; the phosphorus 3.0 mg., and the phosphatase 5.1 Bodansky units per 100 cc.

Stereoscopic x-rays films of the pelvis revealed a multilocular cystic defect with sharply defined borders extending from the crest of the right ilium to the acetabulum (Fig. 1). The bones involved

intravenous pyelogram showed no evidence of renal pathology; the right ureter was slightly displaced medially in its lower portion, probably by the mass in the right ilium.

An operation was performed on the twelfth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. FREDERIC W. RHINELANDER: We have a twenty-nine-year-old woman with a large multilocular cystic area in the ilium and pain of five

months' duration, which had become very severe at the end. Certain points in the history can be taken as probably being significant. The radiation of the pain down the leg is compatible with sciatica, which suggests a lesion in the region of the pelvis rather than one in the hip itself. The fact that the pain was worse at night is also suggestive of bone pain. The fact that the pain became so extremely severe is rather characteristic of tumor. The roentgen report states that the patient had a large lesion in the ilium. Thus, so far, everything in the history fits in.

She is said to have been a thin woman. There is no mention of weight loss, which, had it been a prominent feature, would probably have been put in the history. The displacement of the weight-bearing axis posteriorly is simply what one would expect with poor posture, and is not significant. The mass was palpable, probably deep in the left lower quadrant, which goes with the x-ray picture of something involving the right ilium. The "café-au-lait spot" was apparently a single pigmented area, which I shall discuss later. The fact that there was no pain on compression of the pelvic brim — that test is done to see if there is involvement of one of the joints of the pelvis — suggests that the lesion did not involve these joints. Straight leg-raising was somewhat limited, indicating tightness in the hamstrings, which goes with any lesion in this area that produces muscle spasm and has no diagnostic significance so far as we are concerned.

The blood picture is normal and does not help. A ++ Sulkowitch test is not significant unless the patient is on a low-calcium diet. This is not mentioned here, so probably that was not done. The Hinton test was negative, and the blood calcium and phosphorus were normal. The phosphatase was at the upper level of normal, or a little bit over by most standards; but with an extensive bone lesion, such as we see here, it would probably be considered normal.

May we see the x-ray films?

DR. MILFORD SCHULZ: This is the cystic lesion. It does not appear to expand the bone markedly and does not involve the hip joint. It is multilocular. There is no place where the cortex seems to be broken through. The edges are quite sharply defined. There is not much reaction of the bone at the periphery of the cystic lesion. I think that one would be quite safe in saying that it is a benign lesion. There are no other apparent lesions in the bone. As the record states, there is no decalcification, which tends to rule out a systemic disease that gives cystic changes in the bone. I do not know whether we can accept the displacement of

the ureter as having anything to do with the lesion in the hip.

DR. WILLIAM B. BREED: Did I understand you to say that the ureter was displaced?

DR. SCHULZ: It is displaced medially at the brim of the pelvis.

DR. RHINELANDER: When these films are put in the stereoscope, one can see large cystic areas that, except for a little area at the wing, extend throughout the ilium.

Concerning the differential diagnosis, the most likely conditions are benign bone cyst, enchondroma, eosinophilic granuloma and giant-cell tumor. The others that should be mentioned are easy to rule out, and we can then come back to the more important ones. There is certainly no evidence of malignant disease. This is a large tumor, with a smooth surface and intact cortex. There is no evidence of infection in the clinical picture or the history. A gumma can occur in this area, but the Hinton test was negative and the x-ray films do not suggest it. Albright's disease¹ was probably thought of when the pigmented area was noted, but there is nothing in the picture to suggest that. The lesion was single and there is no mention of sexual precocity, which probably would have been brought out if that had been a serious consideration. Von Recklinghausen's disease of bone (generalized osteitis fibrosa cystica) is ruled out by the single lesion and by the normal blood calcium and phosphorus.

The age of the patient is against a benign bone cyst (localized osteitis fibrosa cystica). In this disease, most patients are under fifteen, and when it does occur in adults, it is usually a case of long standing that had not been discovered in early life, which is quite compatible with this story. Although pain is an uncommon symptom in benign bone cyst, in cases in which the lesion is so large, considerable pain may be expected. That is compatible with this patient's story of no pain in childhood. Pain may not be noticed in a deep-seated bone where there is not much function going on. The site is distinctly unusual for a benign bone cyst, which usually occurs in the shaft of one of the long bones.

The age of the patient is also against enchondroma, which is generally found in the phalanges; but that has to be considered. A multilocular cyst goes with either benign bone cyst or enchondroma.

Eosinophilic granuloma is distinctly uncommon in adults but it has been reported. The location, however, is rather characteristic. However, the large loculi and the integrity of the cortex in a tumor of obviously long duration are very much against this diagnosis, as they are against enchondroma.

The age goes with giant-cell tumor. The severity of pain is suggestive of this condition, but such a tumor occurs at the epiphyseal ends of the long bones, which rather effectively rules this out.

This is obviously an unusual condition. It does not fit in well with any of the lesions mentioned. It is in an unusual location. I think that it corresponds more with a benign bone cyst than with any of the other conditions. The large loculations that one can see in the stereoscope have the appearance of being empty; there is no evidence of cancellous structure, just the big loculi. The fact that the disease had been going on obviously for a great many years takes it back into the age group of benign bone cyst. It was probably present in childhood, when it was painless, and then reached a stage where it expanded the cortex somewhat. That is compatible with this condition, perhaps more so than with the others I have mentioned. Therefore I shall say that the most likely diagnosis is an extensive, localized, benign bone cyst.

DR. FULLER ALBRIGHT: I should like to vote for enchondroma. It looks much like another case that we have had recently.

CLINICAL DIAGNOSIS

Enchondroma or benign giant-cell tumor of ilium.

DR. RHINELANDER'S DIAGNOSIS

Benign bone cyst of ilium (osteitis fibrosa cystica localisata).

ANATOMICAL DIAGNOSIS

Fibrous dysplasia of ilium.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The lesion at operation was found to be cystic, and at biopsy, the wall of one of the cysts and the cortex showed dense fibrous tissue in which there were many bone spicules and areas of imperfectly calcified bone. The ap-

pearance is characteristic of what has been described by Lichtenstein and Jaffe² as fibrous dysplasia of bone. This is a condition that may affect one or several bones; it is usually unilateral and is believed to be a congenital maldevelopment of the bone-forming mesenchyme. Occasionally degeneration with cyst formation of this fibrous tissue occurs, and that is what probably happened in this case. It is the same condition that Albright¹ has called osteitis fibrosa disseminata, but is limited to one bone. I prefer the term fibrous dysplasia because it indicates both the pathologic anatomy and the etiology and because it lessens the confusion with von Recklinghausen's disease of bone (osteitis fibrosa cystica generalisata).

DR. ALBRIGHT: Then you would call it a bone cyst?

DR. CASTLEMAN: It all depends on what you mean by bone cyst. The term "bone cyst" usually applies to a single-chambered cavity occurring in the shaft of a long bone, close to the epiphysis. Other bone lesions, such as the osteitis fibrosa cystica associated with hyperparathyroidism, fibrous dysplasia and giant-cell tumor, may have cystic changes, but the fundamental condition is not a cyst.

DR. ERNEST M. DALAND: What is the prognosis and treatment?

DR. ALBRIGHT: Very good, I should say. The treatment is symptomatic. When it involves a long bone the treatment is that of giant-cell tumor. You curette out the tumor and fill it with bone chips.

DR. DALAND: There is a difference of opinion about filling with bone chips. We believe that it is unnecessary.

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ready gone to the commanding officers of the various service commands authorizing them, if necessary, to induct into service all such physicians between the ages of thirty-eight and forty-five.

The editorial goes on to state that the increasing tempo of the war effort necessitates an additional six thousand physicians in the armed forces by January 1, 1944. The need for these officers is acknowledged by the War Participation Committee of the American Medical Association and by the Procurement and Assignment Service. Indeed, it is so real that the status of physicians already declared "essential" will probably be reviewed to obtain from civilian life all those who can be spared.

The Journal has always asserted — possibly somewhat optimistically — that induction of physicians would never be necessary. If its faith in members of the medical profession is to be maintained, each physician who has been declared "available" and who has failed to offer his services must reappraise his position with a view to relinishing. If he waits for induction, it is likely that his eventual commission will be minimal, rather than according to his age and experience. Because of the need and because of the traditional patriotic response of physicians at such times, there still seem to be reasonable grounds for believing that "— or else" will be unnecessary.

THE DOCTOR PRESCRIBES A DIET

Just as the medical practitioner must be versatile, treating his patients for their real and apparent illnesses, advising them in misfortune and comforting them in affliction, procuring for them extra fuel oil in the winter and extra gasoline in the summer and prescribing for them additional allowances of rationed foods because of their varied appetites, idiosyncrasies and infirmities, so must he also be independent in thought and action, bold in diagnosis and original in treatment.

Nowhere can these latter virtues be more strikingly illustrated than in the prescription of diets, and never has the diet been a source of greater interest than in these days of apportioned food

"— OR ELSE"

The action implied by two words, "or else," uttered by Mr. Paul V. McNutt at the annual meeting of the American Medical Association in 1942 is apparently about to be taken by the Selective Service System to support the increasing demands of the War Manpower Commission. Married men with families who were engaged in nonessential industries have been inducted into military service, and it seems likely that the physician with dependents who has been declared "available" will be treated in a like manner. In fact, according to an editorial in the August 7 issue of the *Journal of the American Medical Association*, a directive has al-

supplies, of ration books and of red points and blue points. To the physician, as is his due, has been given the responsibility of prescribing foods for persons over and above the amounts allotted after careful studies of the available supplies with the knowledge that, when a limited amount is available, that which is given to one above his allotment must, in theory at least, be taken away from the rest.

The number of extra diets thus prescribed has been not inconsiderable; and although many of these requests can be granted out of hand by local rationing boards, when any question seems to exist concerning the propriety of a request, it is referred to the district branch of the Office of Price Administration. Here, if a doubt still lingers,—and, believe it or not, this office is discharging its difficult and thankless function of food rationing in a fair and intelligent manner,—the matter is referred to an advisory committee of physicians appointed for this purpose by the Council of the Massachusetts Medical Society.

During the last two months well over two hundred such requests have been reviewed by the Boston branch alone, and they illustrate beautifully the independence of thought and freedom from the bonds of tradition that the medical profession enjoys. For one patient, for instance, with duodenal ulcer, 40 pounds of processed foods per month, with no extra meats and fats, were prescribed; for another with the same disease, no extra processed foods, but 56 pounds of meats and fats were required. How true the old saying that one man's meat may be another man's poison! For a patient with gastric ulcer, 15 pounds of processed foods and no meats and fats were requested; for another, 48 pounds of processed foods and 83 of meats and fats for a month's allowance. A patient with hypertension and cerebral anemia apparently requires 180 pounds of processed foods and 55 of meats and fats for the lunar period, and one with partial hemiplegia, 143 pounds of meats and fats alone. Let us hope that the last stricken gourmand will have a butcher's

assistance in carving his daily 4 pounds or so of porterhouse! A patient with gall-bladder disease, however, should receive the laurel wreath for his ability to assimilate 10 pounds per day, or 600 for a two-month period, of processed foods—practically enough to stock a small grocery store.

Processed foods—mainly fruit juices and canned, frozen and dried fruits and vegetables—actually present more of an economic and educational problem than they do a medical one. Meat, cheese and fats, most of which are rationed whether processed or not, are protective foods of greater vital importance. With a clear understanding of the value of such unrationed protein as fish, poultry, milk and eggs, however, it becomes apparent that the generally accepted popular values placed on the red meats are largely esthetic ones.

A general discussion of diet and disease is beside the point. It should be emphasized, nevertheless, that if a reasonable degree of care is spent in apportioning ration points, few patients, regardless of their illnesses, require much in the way of food that their basic rations, together with the unrationed foods available, do not supply. For more detailed practical information the reader is referred to the article by Dr. Stare¹ and the letter of Dr. McLaughlin² in recent issues of the *Journal*.

Physicians, of course, will be besieged by seekers of special privileges. If such privileges are granted too liberally, however, and without particular knowledge of the circumstances, they will simply allow themselves to become the dupes of the unpatriotic, the self-indulgent and the unscrupulous.

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MEDICAL EPONYM

BITOT SPOTS

The true nature of these spots as indications of vitamin deficiency was unknown to their original describer, Pierre A. Bitot (b. 1822), professor of anatomy at the School of Medicine and honorary

surgeon of the Bordeaux hospitals, who published in article, entitled "Mémoire sur une lésion conjonctivale non encore décrite, coïncidant avec l'héméralopie [Account of a Conjunctival Lesion not Previously Described, Coincident with Hemeralopia] in the *Gazette Hebdomadaire de médecine et de chirurgie* (10:284-288, 1863), in which he reported 25 cases. A portion of the translation follows:

The purpose of the present note is to point out . . . the coincidence of hemeralopia with a lesion of the conjunctiva; but this lesion does not involve the region of the pupils, forming rather on the eyeball, and consists not in an inflammation but in a collection of brilliant white points which produces what resembles a pearly or silvered spot at the side of the transparent cornea.

This coincidence has neither been described nor even pointed out in the literature.

R. W. B.

RESOLUTIONS

RESOLUTION ON THE DEATH OF ROBERT TITUS PHILLIPS

The recently reported death in a Japanese prison camp in the Philippines of Major Robert T. Phillips, M.C., A.U.S., at the age of forty-one, came as a distinct shock to his many confreres and friends in New England.

To know "Bob" Phillips was to admire him and cultivate his friendship. Graduating from Tufts College Medical School in 1932 he served as house officer and resident on the Third Medical Service at the Boston City Hospital from July, 1932, to February, 1935, and was appointed junior visiting physician to the Boston City Hospital in December, 1936, resigning in August, 1938 when he left Boston to practice his chosen specialty in Portland.

From his college days he displayed unusual executive ability. When a student at Tufts he founded the William Harvey Society, an organization that has perpetuated his ideals and has provided for Tufts medical students, for more than a decade, lectures and seminars at regular intervals, given by national figures in medicine. He was secretary of the Tufts College Medical School Alumni for many years and was a stimulating influence in the reorganization and development of that body.

As a physician he was especially interested in arthritis and was a member of many medical societies. He was commissioned a lieutenant in the Medical Corps Reserve in December, 1922 and

was called to active duty about six months before Pearl Harbor, being in the Philippines when war was declared. The last word from him was received by his wife on January 6, 1942, and told of the evacuation of Manila. Major Phillips wrote that he expected to go to Bataan, where he was taken prisoner. His parents, widow and four children survive him.

Be it resolved that the members of the Boston City Hospital hereby express their regret at the loss of a former beloved member of the Staff and extend to the members of his family their sincere sympathy.

WALTER T. GARFIELD, *Secretary*
Executive Committee
Boston City Hospital

RESOLUTION ON THE DEATH OF CHARLES MACFIE CAMPBELL

We, the Trustees of the Boston Psychopathic Hospital, hereby record our deepest appreciation of the fine leadership which Dr. Charles Macfie Campbell has given unflinchingly for the good of our hospital service during the last twenty-three years. We have had a continuing opportunity to recognize and to value his admirable professional and personal qualities, and we have been proud of the many national distinctions which he has attained.

Our sense of loss, moreover, includes the poignant realization that a good comrade has passed from us.

We extend our heartfelt sympathy to the family of Dr. Campbell.

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SPECIALISM

To the Editor: It has been called to my attention that, in an article entitled "The Universality of a Specialty," which was read before a student medical society in December, 1942, and published in the June 3 issue of the *Journal*, my statement that "the officer-of-the-day . . . though trained as an allergist or ophthalmologist must

nevertheless operate on any patient with an acute appendix who is admitted to the hospital at night during his tour of duty," is not in accordance with the present practice in the Army or Navy. I am informed that the officer-of-the-day acts in the same way that a surgical resident does. He sees all cases that are admitted to the hospital during his tour of duty and decides as to their disposition within the hospital. He can, if he wishes to do so, subject to the customs and orders peculiar to his own hospital and if such treatment is called for, operate on the case himself, call any other member of the staff in consultation or refer the case to any other member of the staff for operation by the latter officer. In the armed services, just as in civilian hospitals, the majority of residents exercise their prerogatives properly and with proper regard for the well-being and safety of the patients. That such proper regard is not always present in the armed forces any more than it is in civil life is evidenced by the illustrations cited above (which actually happened) and by many other similar instances of errors of commission or omission.

Despite the impropriety of my illustration, I see no reason to alter my conviction—as certain critics have suggested I should—that fundamentally the attitude of the medical department of the armed services is one which, as I stated, "still visualizes the general surgeon as a general specialist." This has to be and is properly so under combat conditions but should and need not be so in this country. In relation to neurosurgery in the Army it has been pointed out that sixteen hospitals have been designated by the Surgeon General as specialized hospitals for the treatment of such conditions. This does not mean that these hospitals receive only neurosurgical cases or that they are staffed exclusively by neurosurgeons. It does mean that somewhat more of the usual equipment and staff than exists in the ordinary general hospital has been made available for this specialty in these locations. Where large numbers of neurosurgical patients are concentrated and where the work is done under the direction of a man who has specialized in neurosurgery in civilian life,—as, for example, in the clinic at the Walter Reed Hospital,—no clinic in civil life can surpass and few can equal the calibre of care provided for such patients. There, the neurosurgeon does neurosurgery and nothing else. In other less active centers, however, this is not so. The neurosurgeon is expected to fill in as a general surgeon when there is nothing to do in his own department. Differences in technic, outlook and training in surgery as opposed to neurosurgery are disregarded. The patient whose abdomen would have been opened and closed in a half hour by the nonspecialist is endangered by the fact that the neurosurgeon, who is trained to a painstaking "puttering" type of operating, takes two hours to do the same thing. On the other hand, the general specialist who approaches a craniotomy in terms of a laparotomy will—as has occurred—lose his patient because of bleeding he has neither the patience nor the knowledge to stop or from postoperative surgical shock or circulatory collapse induced by his mistaken belief in the virtues of speed in operating.

A method of handling neurosurgical patients based on the assumption that a neurosurgeon should be able to act at will either as a competent general or as an equally competent specialized surgeon is, I submit, evidence of the conviction—not of junior officers of the medical de-

partments but of those who make the governing policies of the departments—that general specialism as I have described it in my article is a good thing. Whether that is true or not is a matter of opinion that each reader will decide for himself.

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BOOK REVIEWS

Lymph Node Metastases: Incidence and surgical treatment in neoplastic disease. By Grantley W. Taylor, M.D., and Ira T. Nathanson, M.D. With a foreword by Shields Warren, M.D. 8°, cloth, 498 pp., with 61 illustrations and 117 tables. London: Oxford University Press, 1942. \$8.00.

This is the first book of its kind to be published. The authors are to be commended for assembling a vast amount of information on the subject from the literature, for collecting data from three hospitals treating large numbers of cancer patients and for analyzing the results in such a way that proper conclusions can be made of the correct way to deal with metastasizing cancer.

The cases studied are from the Massachusetts General Hospital, the Collis P. Huntington Hospital and the Pondville Hospital (Massachusetts Department of Public Health). The authors are on the staffs of these hospitals and have participated in many of the operations on which they base their conclusions. During recent years, when this book has been in preparation, they have made detailed studies of the anatomic structures concerned in the dissections, the exact location of the nodes and the best types of incisions for each operation. Excellent drawings have been made of these dissections, and the reader may be assured that those shown are true representations of what was found and done at operation. The set-up of the book is pleasing and the subject matter is well arranged.

Part I deals with the anatomy of the lymphatic drainage areas. It is important to know the course of lymph drainage from various organs, the location of lymph nodes and the mechanism of lymph-node metastasis. Certain types of carcinoma are prone to spread along these channels. If the cancer is to be cured, the local process must be destroyed and the regional nodes must be removed. Again, if a metastatic node is palpated, a proper knowledge of lymph-node metastases allows the surgeon to search back for the primary focus. The various body regions have been studied for the exact location of lymph nodes. They are discussed in groups, such as the occipital nodes, the mastoid nodes and so forth, and their relation in the chain of nodes is brought out. Diagrammatic drawings of these lymph nodes in situ, the nodes numbered according to a key and the anatomic structures marked by legends on the side, are very effective. Lymph nodes of the head, neck, axilla, groin, pelvis, abdomen and thorax are demonstrated.

The regional surgical management of lymph-node metastases is the subject of Part II, in which 5481 cases of cancer are analyzed. In 48 per cent, lymph-node metastases were present. Careful study of these cases in groups is the basis for the conclusions and policies regarding treatment.

Lymph nodes may harbor metastases for some time before they become palpable. There is no close correlation between palpability of nodes and involvement by metastases, particularly when the nodes are small. When dealing with carcinomas of relatively low incidence of metastases, small palpable lymph nodes may be of no significance, however, with carcinomas known to metastasize early and widely, small nodes are of great significance. Nodes of more than a centimeter in diameter are quite likely to show metastases. If nodes are firm in consistency, metastases are likely to be present, although inflammatory or tuberculous nodes may be hard. Extension of the growth through the capsule of the node with resulting fixation usually indicates inoperability.

The time at which dissection is done influences the curability of node metastases. If block dissection can be done at the time of removal of the primary tumor, as in the breast, this is the preferable method. In some cases, such as those of the lip, dissection of the neck should be done as soon as the primary lesion has been treated and the wound healed. Dissection of nodes present for a long time or occurring some time after the removal of the primary lesion gives a much poorer prognosis than if early dissection is done. Prophylactic dissection may be advised even though no nodes are palpable, but the decision rests chiefly on the type of primary lesion.

The writers are skeptical of the value of prophylactic radiation of lymph nodes. They state, "It has not been demonstrated that such treatment prevents or diminishes or defers the occurrence of metastases." Preoperative radiation does, however, interfere with the healing of the operative wound. It is sometimes advocated on the basis of destroying cells spilled at operation, but if the case is properly selected and if adequate operation is carried out there rarely is a recurrence in the operative field. If disease is left behind, radiation should be used; but if not, radiation should be reserved until recurrence takes place. Then sufficient treatment should be given to destroy the lesion.

Operations on lymph node areas are described in Part III. Regional dissection of nodes is not advocated unless the primary lesion has been or can be cured. Fixation of nodes and widespread involvement are usually considered as contraindications to operation. The patient should be carefully prepared for surgery. Deficiencies should be corrected and the operation should be done only when he is in the best possible condition. Block dissections should be carried out with great care. Sharp dissection should be used, with fine silk for ligatures. All serum and air should be expressed from the wounds, and pressure dressings should be applied. Most wounds are drained.

Supraomohyoid dissection is advocated for metastases from lesions of the lip and buccal mucosa and the skin of the central third of the face. The platysma muscle is always removed. The operative mortality among 601 patients in three hospitals was 15 per cent.

Radical neck dissection, with removal of all nodes down to the clavicle, the internal jugular vein and the sternomastoid muscle, as well as all tissues removed in the supraomohyoid dissection, is recommended for metastases from the tongue, floor of mouth and parotid gland. The mortality among 112 patients was 36 per cent.

Axillary dissections are done as part of the routine operation for carcinoma of the breast and for metastases from the arm or upper portion of the trunk. In breast operations, removal of the pectoral muscles is essential

to gain access to the nodes of the upper axilla. When the lesion is on the extremity, transection of the pectoralis major is performed and the inner portion is left on the chest wall. The operative mortality among 1153 patients with carcinoma of the breast was 23 per cent, and that of patients undergoing axillary dissections for other lesions was nearly the same.

Inguinal dissections are advocated for malignant lesions of the lower extremities and for metastases from the anus, perineum and external genitals. Simple dissection is often sufficient if the primary lesion is on the extremity. Radical dissection, with removal of the fat and lymphatics along the external iliacs, is necessary for lesions on the anus or genitals. The operative mortality among 262 patients was 38 per cent. In nearly all the deaths, bilateral dissection was done in one sitting, and in several cases the primary lesion was excised at the same time. The authors advise that operations be done in three stages.

The entire book is well done and fills a very important place in cancer literature.

The Essentials of Emergency Treatment 8°, cloth, 146 pp. New Haven, Conn. Connecticut State Medical Journal, 1942.

The value of this little book to physicians who may be called on to do emergency practice should be great. If it were used by all chief medical officers in the Emergency Medical Service of the Office of Civilian Defense it would certainly be instrumental not only in reducing pain and infection but also in saving lives.

Throughout its chapters, surgical essentials are so clearly and simply presented that the volume is most readable, and the reviewer even ventures to add that it will provide an enjoyable evening's reading by the fireside with one's feet up and the favorite pipe functioning satisfactorily. This is no attempt at levity, but an emphasis of the way in which the material on complex subjects has been presented, without being weighted down by forbidding ultra-scientific data.

It is difficult to pick out any one chapter as being better or more instructive than another—each chapter is in itself so worthwhile reading and digesting. The complexity of wound healing, shock and burns, for example, is presented simply and clearly. One does not have to be a professor of chemotherapy to understand it.

One statement, which now is erroneous, deserves comment. On page 56, in the chapter on burns, the author is discouraged at the lack of civilian plans for the storing of blood plasma. This section was written early in 1942 and at that time little had been done to provide adequate amounts of plasma for civilian use. Now, through the efforts of the Office of Civilian Defense and the United States Public Health Service, sufficient stores of plasma are available throughout the country for any civilian needs that might arise. Certain hospitals have been and are collecting, processing and storing plasma and are distributing their surplus to other hospitals. The Office of Civilian Defense has also allocated many units of plasma to strategic communities.

The authors have done a great service to the medical profession in collaborating in this series of papers. The book should be on the desk—not on the shelf—of every practicing physician, and much of the factual material should be constantly kept in mind. The Connecticut State Medical Journal is to be highly commended for making this material so readily available to the profession.

Human Pathology. By Howard T. Karsner, M.D. Sixth edition. 4°, cloth, 817 pp., with 460 illustrations in black and white and 24 subjects in color on 16 plates. Philadelphia: J. B. Lippincott Company, 1942. \$10.00.

The sixth edition of Karsner's textbook has appeared approximately at the same time as the seventh edition of W. G. MacCallum's textbook and the fifth edition of Sir Robert Muir's textbook.

In spite of the fact that Karsner's book is shorter than that of MacCallum and that it does not go so deeply into the details of descriptive pathology as does Muir's book, it is in many respects equal to either. It deserves to be recognized as one of the three standard works in pathology of our time. Its especially valuable feature is the bibliography at the end of each chapter. There is evidence of profound knowledge and excellent choice, valuable not only for the beginner but for the mature pathologist. In many respects Karsner's book is a bonanza, demonstrating the wide experience, the close observation and the sound judgment of the author. Two good examples of this are the discussion covering the persistence of cartilage discs between the vertebrae in cases of pulsating and excavating aneurysms of the aorta and that regarding the reactivation of latent syphilis by the intercurrent of acute infections.

But it is the duty of a reviewer to find some grounds for adverse criticism. It would seem better to consider infectious mononucleosis in the chapter on infectious diseases than with the diseases of the reticuloendothelial system. If the heterophile antibodies are mentioned, their interference with the Wassermann reaction by giving a nonspecific positive should be mentioned. Although undulant fever is one of the diseases rarely seen by the pathologist at autopsy and although but few references to autopsy findings are found in the literature, it deserves mention in a textbook of pathology. In the chapter on glanders, since testicular foci are practically pathognomonic, they should be mentioned, especially because the edema of the seminal cord in infected animals is cited by the author. Agenesis of the kidneys is not limited to monsters.

In general, it may be said, that the sixth edition deserves to acquire new friends among students and doctors. For coming editions one might suggest a more elaborate description of certain aspects of pathology, for example, the biologic and structural peculiarities of infancy and old age.

The Dynamic State of Body Constituents. By Rudolf Schoenheimer, M.D. 8°, cloth, 78 pp., with 16 tables. Cambridge: Harvard University Press, 1942. \$1.75.

In considering reactions taking place within the living body, many substances long held to be relatively stable have been shown of late to be subject to reversible equilibria. Schoenheimer has characterized this situation as "a steady state of rapid flux."

Much of the experimental work leading to this radically new concept has made use of isotopically labeled compounds. Schoenheimer, a leading experimenter with the stable isotopes, summarized the most critical of his experiments and the sequential physiologic conclusions for the Dunham Lectures of October, 1941. The majority of the experiments utilize food stuffs (fats or amino acids) or metabolic intermediates (arginine or creatine) marked with introduced isotopes of hydrogen or nitrogen. Some few of the studies are startling in their simplicity. Fast-

ing rats were, for example, injected with heavy water, and deuterium was found in all the amino acid fractions, except lysine, isolated from the animal's proteins twenty-four hours after the injection. For the details of the more complicated studies the original book should be consulted. The activity of glutamic acid in reversible dehydrogenations and in transaminations is repeatedly emphasized.

Death intervened before the lectures were delivered; Dr. Schoenheimer's colleagues completed the necessary revisions. Dr. Hans T. Clarke presented the lectures, which appear in this small volume.

Psychiatry in Medical Education. By Franklin G. Ebaugh, M.D., and Charles A. Rymer, M.D. 8°, cloth, 643 pp., with 16 tables and 7 charts. New York: The Commonwealth Fund, 1942. \$3.50.

The authors have made a complete survey of the teaching of psychiatry in medical schools in this country, both to undergraduates and postgraduates. They have also examined the teaching facilities in general as well as special hospitals. The various methods of teaching are analyzed. A marked variation in methods of instruction in colleges and hospitals was found; no uniform agreement in regard to how psychiatry ought to be taught exists. Some schools give reasonably satisfactory courses, but in many the instruction is poor and inferior. Since psychiatric teaching is in a confused and unsatisfactory state, the needs for this survey are clearly indicated. Emphasis is rightfully put on the value of personality studies and the treatment of the whole patient—a total person with a mind as well as a body.

For the teacher of psychiatry, there is important material in the appendices to this book. The "personality study" used at the Johns Hopkins University School of Medicine and elsewhere is given in full. An outline of lectures in psychiatry and a list of central agencies for the direction of state institutions will also be found useful.

The book, in general, is adequate in every respect. From its use should come important advances in the teaching of psychiatry in the United States and elsewhere.

Ovarian Tumors. By Samuel H. Geist, M.D. 8°, cloth, 527 pp., with 312 illustrations. New York: Paul B. Hoeber, Incorporated, 1942. \$10.50.

This monograph is a thorough résumé of knowledge of ovarian tumors up to 1936. The embryology, anatomy and physiology are considered in some detail. There follows a discussion of each group of ovarian tumors represented in the classifications of Pfannenstiel, Sternberg, Goodall and Meyer. The references, which are many, include practically all the foreign articles on the subject but few references to American reports or investigations.

The book lacks an adequate discussion of the laboratory findings in cases of endocrine tumors of the ovaries, such as, reports of 17-ketosteroid and follicle-stimulating-hormone determinations, reports of the amount of estrin in the fluid of follicle cysts and so forth. There is some discussion of the problem, however, in the section on granulosa-cell tumors of the ovary.

This book is a satisfactory review of Dr. Geist's vast experience and of the foreign literature and, as such, is a valuable addition to knowledge of the ovarian neoplasms.

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THE DIFFERENTIAL DIAGNOSIS OF CHRONIC BRIGHT'S DISEASE*

A Clinicopathological Correlation

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BOSTON

IT IS quite apparent to clinicians that the task of correctly foretelling the pathological findings in cases of advanced renal disease is difficult and may be impossible, since the end results of many types of renal disease may be similar so far as the clinical picture is concerned. Although much work on renal physiology and pathology has been reported in recent years, the studies that have approached the problem from the viewpoint of the clinician faced by a patient with hypertension and failing renal function are few in number, and those that have been made have for the most part paid little attention to chronic or healed pyelonephritis as an important type of chronic Bright's disease.

There exists, moreover, considerable confusion in the clinical and pathological nomenclature of Bright's disease, largely owing to the many different classifications of nephritis that have been in use. To some extent this is, as Christian¹ states, "more a matter of difference in words than in concepts." It is for the most part agreed that in one group vascular lesions predominate; in a second, diffuse inflammatory glomerular lesions are chiefly present; whereas in a third, degenerative changes in tubules and glomeruli are the outstanding features. A fourth type, however, also exists in which the lesions are mainly interstitial and originally infectious. Within recent years it has been shown and emphasized by Longcope and Winkenwerder,^{2,3} Peters, Laviettes and Zimmerman,⁴ Butler⁵

Weiss and Parker⁶ and others that renal infection—that is, pyelonephritis—may ultimately result in hypertension, often of the malignant type, as well as in renal failure. These late sequelae may occur even when the original infection has subsided and healing has taken place.

The pathological findings as well as the clinical manifestations of the various types of Bright's disease have been described on numerous occasions,^{1-4, 6-14} and no attempt will be made here to summarize the literature. Brief comment is, however, called for on the term "malignant hypertension," about which much confusion exists. As originally applied by Fahr,¹⁰ "malignant nephrosclerosis" was the pathological description of the kidneys of patients dying of uremia in which hyperplastic endarteritis and necrotizing arteriolitis were present. Later the problem was approached primarily from the clinical angle, and Keith, Wagener and Kernohan¹⁵ applied the designation "malignant hypertension" to a syndrome of severe hypertension with retinitis and papilledema, progressing rapidly to a fatal termination. Although many such patients died in uremia, some succumbed to cardiac failure or cerebral accident. The latter cases usually exhibited pathologically the same general type of renal lesion as that described by Fahr, but often to a less severe extent than those in which death was primarily due to renal failure.

It has been subsequently shown that malignant hypertension as seen clinically does not represent a single pathologic entity, but may occur as the terminal phase of benign essential hypertension, chronic glomerulonephritis or healed or chronic pyelonephritis, as well as rarely in conditions such as renal infarction and congenital polycystic kidneys.^{6, 10, 17}

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CHOICE OF MATERIAL

In the present analysis only the commoner types of chronic renal disease that often terminate in uremia are considered. No analysis has been made of the degenerative renal diseases, such as nephrosis and amyloid disease, of congenital anomalies, of renal tuberculosis or of obstructive lesions without infection.

The cases were originally selected from the autopsy files of the Boston City Hospital and represent consecutive cases of each type, with the exclusion of those in which the pathological diagnosis was not clear, those with some other major disease that might complicate the interpretation of the clinical picture, such as heart disease of other etiology, and those in which there were insufficient clinical data. An exception was made only in cases of decompensated benign nephrosclerosis, for in this group only those patients with benign nephrosclerosis dying in uremia were included, which of course left out the vast majority of patients with essential benign hypertension. The selection and classification were therefore made on the basis of pathological findings.

The clinical studies were such as might be expected to be made routinely on the wards of a large general hospital and varied in extent and probably in accuracy. A few patients were personally observed by us.

CLASSIFICATION

This study has been limited to the three commoner large groups of chronic nephritis, each of which has been subdivided in the following manner:

- I. Glomerulonephritis
 - a. Subacute
 - b. Chronic
- II. Nephrosclerosis
 - a. Benign
 - b. Malignant
- III. Pyelonephritis
 - a. Healed
 - b. Chronic

Although the concept of glomerulonephritis is an old and broadly accepted one, it is probable that many of the lesions that were so diagnosed in the past would now be called some stage of pyelonephritis or malignant nephrosclerosis. The concept of glomerulonephritis should be restricted, in our view, to lesions in which the primary change is a diffuse involvement of the glomeruli by an active or healed inflammatory process. Cases with

a prolonged course can be divided more or less into two stages, usually known as subacute and chronic, although the dividing line is not a sharp one. In Table 1 are given the gross and microscopical criteria used for such separation, as well as the characteristic features of the other renal lesions under discussion.

Nephrosclerosis includes that group of kidneys in which the first and fundamental change is an arteriolar sclerosis. It has been suggested by Arthur Ellis,⁹ who bases his conception on the experimental work of Wilson and Byrom,¹⁸ that these changes are probably the result rather than the cause of an associated hypertension. A similar point of view is taken by Dock,¹⁹ who summarizes the arguments in its favor. There is, however, another school of thought that maintains that renal arteriolar sclerosis is the primary disease, the hypertension resulting from the renal ischemia. This is the belief of Scott,²⁰ and it is at least assumed by Goldblatt, Kahn and Lewis²¹ in a summary of the treatment of experimental hypertension.

As a result of the renal arteriolar lesions, changes are produced in the kidney that may or may not, according to their degree, lead to renal decompensation. Pathologically the distinction between benign and malignant nephrosclerosis is made mainly on the basis of the type of arteriolar sclerosis present. In the benign form this is chiefly hyaline in type, the hyaline thickening of the wall leading to marked narrowing or even complete occlusion of the vessel. In malignant nephrosclerosis the arteriolar sclerosis is hyperplastic in type, the lumens being narrowed or occluded by a proliferation of cells, probably fibroblasts, between the muscularis and the endothelium. Necrosis of the wall with hemorrhage into it, polymorphonuclear infiltration and fibrin deposition (necrotizing arteriolitis) often occur but are not so pathognomonic of the condition as is the hyperplastic change. Other gross and microscopical criteria are given in Table 1.

Not uncommonly borderline cases with combinations of the features of benign and malignant nephrosclerosis are found. Most of these patients are between fifty-five and sixty-five years of age and clinically are usually considered as examples of the malignant form.

Our conception of pyelonephritis is essentially that of Weiss and Parker.⁶ The important gross and histologic characteristics are given in Table 1. The vascular picture is somewhat complicated. As shown by Weiss and Parker, hyperplastic arteriolar sclerosis may be restricted to those areas where the inflammatory process was originally present.

In the cases associated with hypertension, however, arteriolar sclerosis, usually hyperplastic in type, is present not only in the scarred areas but throughout the kidneys and also in other organs of the body. This diffuse process is probably best explained as caused by the hypertension.

The separation of chronic pyelonephritis from healed pyelonephritis is not an easy one, particularly from the purely pathological standpoint. It depends on one's being able to find evidence of active infection still present in the lesions. Such

or significant hypertension exceeded the number with subacute or chronic glomerulonephritis, as has been pointed out by Weiss and Parker.⁶

Essential hypertension, of course, occurs with great frequency, but the number of cases classed as decompensated benign nephrosclerosis is less than the incidence of malignant nephrosclerosis.

Age at Death

It will be seen from Table 2 that subacute and chronic glomerulonephritis, malignant nephro-

TABLE 1. *Gross and Microscopic Characteristics of the Kidneys in Chronic Bright's Disease.*

CHARACTERISTICS	SUBACUTE GLOMERULONEPHRITIS	CHRONIC GLOMERULONEPHRITIS	BENIGN NEPHROSCLEROSIS	MALIGNANT NEPHROSCLEROSIS	HEALED PYELONEPHRITIS	CHRONIC PYELONEPHRITIS
Gross	Large or normal, pale yellow, smooth to granular.	Pale, contracted, granular.	Contracted, granular, prominent blood vessels	Slightly contracted, mottled pale and red, petechial hemorrhages	Coarsely scarred or very contracted and granular	Coarsely scarred or very contracted and granular, abscesses (?).
Microscopic						
Involvement	Diffuse	Diffuse	Focal	Focal	Focal or diffuse	Focal or diffuse
Glomeruli	Fresh crescents, increased cellularity.	Old crescents, adhesions, fibrosis	Normal to fibrotic	Normal, infarcted, necrotic or inflammatory	Reduced in number, pericapsular fibrosis	Reduced in number, pericapsular fibrosis
Tubules	Fatty degeneration	Atrophy and dilatation	Atrophy and dilatation	Hyaline droplets, fatty degeneration	Thyroid like areas	Thyroid like areas, with polymorphonuclear leukocytes in some
Interstitial tissue	Edema; doubly refractile fat.	Fibrosis	Fibrosis	Perivascular lymphocytic infiltration	Fibrosis, lymphocytic infiltration.	Fibrosis polymorphonuclear, lymphocytic and plasma-cell infiltration.
Blood vessels	Hyaline or hyperplastic arteriolar sclerosis	Hyaline or hyperplastic arteriolar sclerosis	Hyaline arteriolar sclerosis, atherosclerosis of arteries.	Hyperplastic arteriolar sclerosis, necrotizing arteriolitis	Hyaline or hyperplastic arteriolar sclerosis	Hyaline or hyperplastic arteriolar sclerosis

evidence usually consists of the presence of leukocytes in the interstitial tissue or in the lumens of the tubules. Sometimes even organisms can be demonstrated.

RESULTS

Relative Incidence

Since the cases studied were a selected group, they are not indicative of the relative incidence of the various types of chronic Bright's disease. Healed pyelonephritis, as judged from the presence of old scarring of the kidney, is of common occurrence. A recent study of Kinney and Mallory,²² as yet unpublished, based on 1000 consecutive post-mortem examinations at the Boston City Hospital, indicates that it may occur in nearly 14 per cent of all persons. Many of these lesions were minor in degree, and in life the patients had few or no clinical manifestations referable to their kidneys. Nevertheless the number of patients who had disease of such degree as to lead to renal failure

sclerosis and healed pyelonephritis in this series are diseases of youth and early middle age.

Predisposing Factors

Infection appears to bear a definite relation to glomerulonephritis. All but 1 of the patients with subacute glomerulonephritis and 6 of those with chronic glomerulonephritis had scarlet fever, sore throat or some other respiratory infection preceding the onset of symptoms. On the other hand, a clear-cut history of acute glomerulonephritis or of acute pyelonephritis was rarely elicited in the patients with chronic glomerulonephritis and with healed or chronic pyelonephritis, respectively. A history of toxemia of pregnancy occurred in only 2 cases, both in the healed pyelonephritis group.

Abnormalities of the urinary tract were not found in any group except that of pyelonephritis. One patient with healed pyelonephritis had a unilateral renal calculus with some hydronephrosis. Of the 6 cases of chronic pyelonephritis 1 patient

showed unilateral renal calculus with hydronephrosis; 1, an infant of eight months, had hydroureters; and 1 had prostatic obstruction.

Known Duration of Renal Disease and of Hypertension

The known duration of renal disease and of hypertension as judged from the records is proba-

disease for two and a half, three and six years, respectively. In the other groups the known duration varied from a few months to many years.

Terminal Arterial Blood Pressure

Figure 1 shows the average range of blood pressure for each patient during his terminal illness. The marked hypertension, especially diastolic, was

TABLE 2. Summary of Clinical Data, Chiefly Expressed as Frequency of Occurrence.

DIAGNOSIS	NO OF CASES	AGE AT DEATH	DURATION OF RENAL DISEASE OR HYPERTENSION	PREDISPOSING INFECTIONS	TERMINAL URINE			
					++++ ALBUMIN	W. B. C.	R. B. C.	
		yr.		%	%	%	%	
Subacute glomerulonephritis . . .	10	16-43 (mean, 30)	1 mo.-6 yr.	90	100	100	100	
Chronic glomerulonephritis . . .	10	21-46 (mean, 35)	6 mo.-13 yr.	60	70	100	67	
Decomp. benign nephrosclerosis	11	48-80 (mean, 63)	1 mo.-12 yr.	18 (?)	0	100	33	
Malignant nephrosclerosis	11	27-51 (mean, 42)	2 mo.-4 yr.	0	55	90	37	
Healed pyelonephritis	11	24-92 (mean, 40)	1 mo.-30 yr.	18 (?)	45	80	30	
Chronic pyelonephritis	6	2/3-77 (mean, 45)	6 mo.-20 yr.	0	50	100	84	

	NEPHROTIC SYNDROME	ANEMIA	TERMINAL UREMIA	TERMINAL BLOOD PRESSURE	PAPIL-LEDEMA	HYPERTENSIVE ENCEPHALOPATHY	CEREBROVASCULAR ACCIDENT	HEART FAILURE	TERMINAL HEART FAILURE
	%	%	%		%	%	%	%	%
Subacute glomerulonephritis	90	70	80	125/70-190/146 (mean, 170/100)	50	10	0	40	10
Chronic glomerulonephritis	30	100	100	200/110-260/160 (mean, 200/130)	29	38	30	60	60
Decomp. benign nephrosclerosis	0	72	100	160/90-275/150 (mean, 220/135)	27	18	9	81	64
Malignant nephrosclerosis	0	54	90	205/120-260/165 (mean, 240/150)	90	72	18	90	54
Healed pyelonephritis	0	54	90	90/60-210/150 (mean, 210/130)	78	54	27	45	9
Chronic pyelonephritis	0	50	100	105/80-270/130 (mean, 140/90)	25	0	0	37	17

bly an inaccurate indication of their actual duration. Nevertheless, it is of interest. In benign nephrosclerosis, known hypertension was frequently diagnosed some years before renal disease, whereas in the other groups renal disease was diagnosed initially or the hypertension and renal disease were first observed at the same time.

The relatively short duration of the known disease in malignant nephrosclerosis is striking, only 1 patient living three years after a diagnosis was first made, and the rest dying within two years. The duration of disease in subacute glomerulonephritis is also usually short (one year or less), although 3 patients were known to have had the

consistently seen in malignant nephrosclerosis and was often but not always encountered in benign nephrosclerosis and chronic glomerulonephritis. In subacute glomerulonephritis and in healed pyelonephritis the ranges of pressure were wide, whereas only 1 case of chronic pyelonephritis exhibited well-marked hypertension.

Retinal Findings

Retinal findings were variously described in the records. An attempt has been made to classify them in a general way according to the terminology of Wagener and Keith.¹⁴ Grade 4 changes consist of papilledema, usually with other severe

manifestations of retinal and vascular changes as well. This so-called "hypertensive neuroretinopathy" is generally agreed to constitute a grave prognostic sign, and by many its presence is considered to merit a diagnosis of malignant hypertension. Although 9 of the 10 cases of malignant nephrosclerosis in which the eyegrounds were ex-

type, since it was absent in 2 cases and of slight degree in several others. Conversely, marked microscopic pyuria may occur in lesions of other types than pyelonephritis.

Too few tests for bacteriuria and pyelographic examinations were made to merit analysis. Such studies might in some cases have been of diagnos-

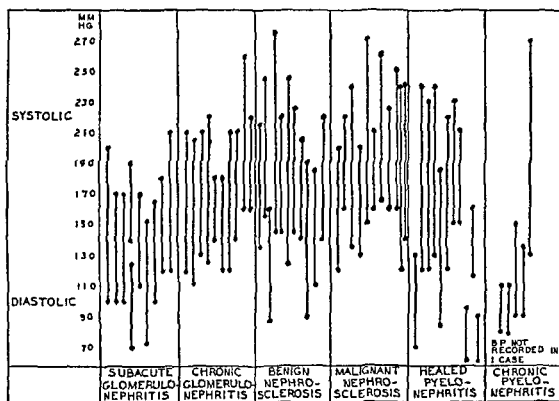


FIGURE 1. Average Blood-Pressure Readings in Various Types of Chronic Bright's Disease at Time of Last Hospital Entry.

amined showed papilledema, it is of great interest that 7 of 9 cases of healed pyelonephritis had similar fundal changes, and they occurred in one or more cases of each of the other groups. Hence, although the pathologic entity, malignant nephrosclerosis, almost invariably presents the clinical picture of malignant hypertension, the converse is not true. Clinical malignant hypertension, as judged especially by retinal changes, not only is produced by malignant nephrosclerosis, but often occurs in healed pyelonephritis and may be found in any of the types of nephritis discussed here.

Urinary Findings

As shown in Tables 2 and 3, no pattern of urinary findings is pathognomonic of any one type of nephritis. However, marked proteinuria, hematuria, pyuria and cylindruria occurred with great regularity in subacute glomerulonephritis and almost as often in chronic glomerulonephritis. Malignant nephrosclerosis presented a picture ranging from an almost normal urine to one resembling that of glomerulonephritis; the same was true of benign nephrosclerosis, although severe changes were uncommon.

Although pyuria was always present in chronic pyelonephritis, this was not true in the healed

type help, but it should be pointed out that in our experience, as well as that of others, pyelonephritis may exist with normal pyelographic findings and, at least in the healed type, without bacteriuria.

Few patients were followed in this hospital over a long period with careful studies of their urine. However, in those who were so followed it was apparent that in glomerulonephritis gross urinary abnormalities were present early in the course of the disease, often before the development of significant hypertension. The changes persisted, although terminally the albuminuria and abnormalities in the sediment occasionally diminished slightly in amount.

In contrast, patients with nephrosclerosis frequently exhibited comparatively little in the way of urinary abnormalities until late in the disease. The patients with healed pyelonephritis did not follow a consistent pattern. In some of these cases, as in nephrosclerosis, the urine was normal or nearly so for long periods of time, whereas in others persistent or intermittent pyuria occurred and microscopic hematuria was occasionally found.

Leukocyte Count

Leukocytosis of some degree was present in almost all cases at some time.

Nephrotic Stage

By the term "nephrotic stage" is meant the clinical syndrome in which generalized edema, usually

TABLE 3. Summary of Urinary Findings at Terminal Hospital Admission.

URINARY FINDING	No OF CASES				TOTAL No OF CASES
	0	+ TO +++	++	++	
Proteinuria					
Subacute glomerulonephritis	0	0	10		10
Chronic glomerulonephritis	0	3	7		10
Malignant nephrosclerosis	0	5	6		11
Benign nephrosclerosis	1	10	0		11
Healed pyelonephritis	1	6	4		11
Chronic pyelonephritis	0	3	3		6
	0	+ TO +++			
Hematuria (microscopic)					
Subacute glomerulonephritis	0	9			9
Chronic glomerulonephritis	2	4			6
Malignant nephrosclerosis	7	4			11
Benign nephrosclerosis	6	3			9
Healed pyelonephritis	7	3			10
Chronic pyelonephritis	1	5			6
	0	+ TO +++			
Pyuria					
Subacute glomerulonephritis	0	10			10
Chronic glomerulonephritis	0	9			9
Malignant nephrosclerosis	1	9			10
Benign nephrosclerosis	0	7			7
Healed pyelonephritis	2	8			10
Chronic pyelonephritis	0	6			6
Cylindruria					
Subacute glomerulonephritis	9	5	0		10
Chronic glomerulonephritis	5	2	1		10
Malignant nephrosclerosis	7	1	4		11
Benign nephrosclerosis	4	0	2		11
Healed pyelonephritis	6	0	0		11
Chronic pyelonephritis	1	0	1		6

This type of edema is related to hypoproteinemia and marked proteinuria. Consistent with this is the fact that the plasma protein of 7 of 9 patients with subacute glomerulonephritis was below 5 gm. per 100 cc. during the last part of their stay in the hospital, and in no other group were protein levels below 5 gm. found. The patients with subacute glomerulonephritis either showed nephrotic edema at the time of death or had had it in the recent past. Those with chronic glomerulonephritis had exhibited edema months or years prior to death.

In 2 of the cases of subacute glomerulonephritis with nephrotic edema, the edema cleared in the weeks before death as renal failure advanced; in the other 7, however, it persisted. In 3 of these cases mild heart failure occurred in the late stages of the disease.

Edema that was not clearly cardiac occurred in 2 patients with malignant nephrosclerosis and in 1 with healed pyelonephritis, but this edema was mild and may well have been due to other than renal causes.

Renal Failure (Uremia)

If one takes as a rough measure of uremia the presence of a blood nonprotein nitrogen above 60 mg. per 100 cc.,—not due to extrarenal causes,—all the patients in all groups suffered from it during their terminal hospital stays, with the exception of 2 cases of subacute glomerulonephritis and 1 each of malignant nephrosclerosis and healed pyelonephritis (Tables 2 and 4). Even these 4 patients had nonprotein nitrogen levels above 50 mg. at some time during their final stay in the hospital. The degree of nitrogen retention was studied but

marked in degree, dominates the picture. There was no known nephrotic stage in any of the disease groups except those of subacute and chronic

TABLE 4. Cause of Death in Cases of Chronic Bright's Disease.

CAUSE OF DEATH	SUBACUTE GLOMERULO- NEPHRITIS	CHRONIC GLOMERULO- NEPHRITIS	BENIGN DECOM- PENSATED NEPHRO- SCLEROSIS	MALIGNANT NEPHRO- SCLEROSIS	HEALED PYELO- NEPHRITIS	CHRONIC PYELO- NEPHRITIS
Uremia						
Uremia and contributory heart failure	8	3	4	3	7	4
Uremia and heart failure	0	2	2	4	1	1
Heart failure and contributory uremia	0	3	5	2	0	0
Cerebral accident and uremia	0	1	0	0	1	0
Heart failure and toxemia of pregnancy	0	1	0	1	1	0
Cerebral accident	1	0	0	0	0	0
Nephrosis and bronchopneumonia	0	0	0	1	1	0
Peritonitis and postoperative shock	1	0	0	0	0	0
	0	0	0	0	0	1*

*No determination of blood nonprotein nitrogen done.

glomerulonephritis. In the subacute group it was present in 9 of 10 cases, lasting from a month to a year. In the chronic group it occurred in only 3 of 10 cases.

showed nothing characteristic in the different groups.

In our series the absolute duration of the renal failure frequently could not be told, since many of

the cases came under observation only at a time when uremia was already present. However, from the known duration of uremia shown in Figure 2 it can be seen that uremia of relatively long duration is common in glomerulonephritis and benign

and 4. It was commonest in patients with decompensated benign nephrosclerosis, where, in spite of the fact that only cases involving death in uremia were chosen, 7 of 11 had significant degrees of heart failure. Moreover, it occurred frequently in

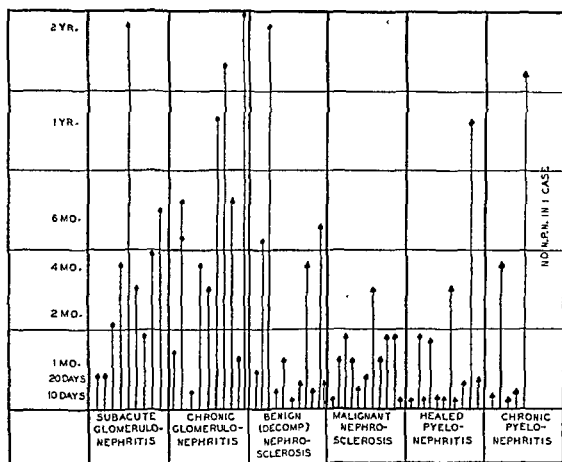


FIGURE 2. Known Duration of Nitrogen Retention (above 60 mg. per 100 cc.) in Various Types of Chronic Bright's Disease.

nephrosclerosis and may occur in pyelonephritis.

Tests designed to show early diminution in renal function, such as concentration tests, phenolsulfonphthalein excretion, clearance tests and so forth, were done too infrequently to be of value in this study.

Anemia

In general the anemia was of a normocytic type and tended to be related to the degree and especially the duration of renal failure. In 2 cases anemia of this type had existed for three months before the nitrogen retention exceeded 60 mg. per 100 cc., and in 2 cases nitrogen retention of this amount or more had persisted for twelve and twenty-four months, respectively, before anemia occurred, but in all other cases the known durations of anemia and of nitrogen retention tended to parallel each other, and in every case in which anemia did not occur the known uremia had existed for six weeks or less.

Heart Failure

The importance of heart failure as a primary or contributing cause of death is shown in Tables 2

chronic glomerulonephritis and malignant nephrosclerosis.

Hypertensive Encephalopathy

Table 2 shows the incidence of this manifestation, which was taken to include episodes of blurred vision, transitory loss of consciousness, aphasia, transient paralysis and so forth. It appeared to be correlated to some extent with the degree of hypertension or of generalized vascular disease or both.

Cerebral Accidents

The occurrence of cerebrovascular accidents is shown in Table 2. In both cases of malignant nephrosclerosis, in 2 cases of healed pyelonephritis and in 1 case of chronic glomerulonephritis the cerebral episodes were the chief immediate cause of death (Table 4).

DISCUSSION

The clinical manifestations in the advanced stages of chronic Bright's disease are not specific for different pathological types. This has been pointed out before by others, but requires re-

emphasis since there still exists confusion in the minds of many. These clinical manifestations are in the main dependent on either failing renal function or arterial hypertension and its sequelae or both. A lesion of any type if sufficiently severe, diffuse and long lasting may so damage the kidney as to cause its function to fail, and when renal failure occurs the clinical picture tends to conform to a certain general pattern regardless of the initiating cause.

Moreover, it is also increasingly evident that many types of renal disease may be accompanied by chronic hypertension, that this hypertension may be of any degree of severity, and that when it is once established the complications that occur are those of chronic hypertension and its associated vascular disease, and are not dependent on the primary causative factor. In certain types of nephritis—for example, glomerulonephritis and pyelonephritis—there is good reason to believe that the renal factor is of primary importance in producing the hypertension. In nephrosclerosis, on the other hand, there is as yet no good evidence that the renal pathologic changes are not secondary to a preceding hypertension of unknown etiology, although once established a vicious circle may be set up, so that the renal ischemia resulting from the nephrosclerosis may aggravate the arterial hypertension, which in turn increases the pathologic change within the kidney.

There are, however, certain features in the life history of the different varieties of chronic nephritis that occur with greater frequency in one type than in another, and there are a few clinical manifestations that are to be found in one type only. Hence the attempt of the clinician to make a diagnosis based on the underlying pathology is not entirely fruitless, since in many cases a proper evaluation of the various clinical factors should lead to the correct diagnosis.

The clinical findings can best be evaluated and understood in the light of the present knowledge of the pathogenesis of the various types of chronic nephritis. Thus, although the fundamental etiology of nephrosclerosis is unknown, it is clear that in the fully developed state there is evidence of widespread vascular disease, and that the malignant type differs from benign nephrosclerosis in the severity of the changes and the rapidity with which they occur. It is obvious, therefore, why nonrenal manifestations, especially in the brain, are commoner in nephrosclerosis, particularly the malignant type, than in the other groups. In malignant nephrosclerosis it is not uncommon for failure of the kidneys, heart and cerebral circula-

tion to occur almost simultaneously. As emphasized by Weiss and Parker,⁶ widespread vascular disease is infrequent in patients with hypertension secondary to pyelonephritis.

Several factors combine to produce strain on the heart in chronic nephritis: the height of the blood pressure; the duration of the hypertension; coronary vascular disease; the anemia, which lowers the oxygen-carrying power of the blood and tends to produce an increased cardiac output; and the toxic effect of the uremia on the myocardium. Hence it is not surprising that heart failure occurs so frequently in all groups.

The renal lesion is most obviously present and dominant in glomerulonephritis, and in this group, findings directly related to renal involvement are most constantly present. A striking finding in our series was that the nephrotic syndrome occurred only in glomerulonephritis.

The only variety of Bright's disease that usually runs a characteristic clinical course easily distinguishable from the other types is subacute glomerulonephritis. The onset can most often be definitely dated following an upper respiratory infection, and may be typical of acute nephritis. Occasionally there is a subsequent interval when the patient is free of symptoms, with one or more relapses following further respiratory infections, but frequently the course is progressive from the onset, with nephrotic edema dominating the picture and death ensuing in a few months to a few years. Increasing impairment of renal function takes place, followed by uremia, sometimes hastened by intercurrent infections. The manifestations and complications of hypertension are ordinarily less striking in this type of nephritis than in the others, although even here some degree of heart failure is not infrequent in the late stages.

Whether it is justified on either clinical or pathological grounds to classify subacute separately from chronic glomerulonephritis is open to question. All gradations between the two types exist. The disease is considered subacute when it has progressed so rapidly that death occurs before scarring, and hypertension with its vascular changes takes place to a significant or dominating degree. Conversely, in chronic glomerulonephritis the initial renal lesion is often not so extensive as to produce the nephrotic syndrome or so overwhelming as to result in early death, but does result in renal changes leading to hypertension. There is thus initiated the vicious circle of hypertension and vascular renal change already mentioned. In any case the term "subacute" is an unfortunate one, since this stage of the disease may last for years.

SUMMARY AND CONCLUSIONS

A clinicopathological study has been made of chronic Bright's disease, comprising (as defined by post mortem examination of the kidneys) 10 cases of subacute glomerulonephritis, 10 of chronic glomerulonephritis, 11 of decompensated benign nephrosclerosis, 11 of malignant nephrosclerosis, 11 of healed pyelonephritis and 6 of chronic pyelonephritis.

Glomerulonephritis, malignant nephrosclerosis and healed pyelonephritis terminated in youth and early middle age, benign nephrosclerosis occurred after fifty, and chronic pyelonephritis was found at all ages.

An acute onset following respiratory infections usually occurred in subacute glomerulonephritis but was recorded much less often in chronic glomerulonephritis. A history of acute pyelitis was rarely elicited in the pyelonephritic cases.

The known duration of disease was usually relatively short in malignant nephrosclerosis (two years or less, with one exception), in the other conditions the range of duration was much greater

In malignant nephrosclerosis, terminally a well marked arterial hypertension was consistently present, and this also usually occurred in benign nephrosclerosis, healed pyelonephritis and chronic glomerulonephritis.

Nine of 10 cases of malignant nephrosclerosis and 7 of 9 cases of healed pyelonephritis showed reinitis with papilledema. This also occurred in 25 to 50 per cent of the cases in the other groups.

There is no pattern of urinary findings pathognomonic of any one type of nephritis. In healed pyelonephritis the urinary findings may be minimal, and pyuria may be absent.

The nephrotic syndrome occurred only in glomerulonephritis.

Renal failure occurred in all cases, although in 2 cases of subacute glomerulonephritis and 1 each of malignant nephrosclerosis and healed pyelonephritis it was minimal. Uremia of relatively long duration is frequent in glomerulonephritis and benign nephrosclerosis and may occur in pyelonephritis. Anemia tended to be related to the degree and especially the duration of renal failure.

Heart failure occurred commonly in all groups

and with great frequency in both types of nephrosclerosis. It was often the primary or an important contributory cause of death.

Cerebrovascular symptoms were apparently related to the degree of hypertension or of generalized vascular disease or both, and were commonest in malignant nephrosclerosis.

The clinical manifestations in advanced stages of chronic Bright's disease are not specific for different pathological types. They are, in the main, dependent on failing renal function or on arterial hypertension and its sequelae or both. There are, however, certain features in the life history of the different types of Bright's disease that occur with greater frequency in one type than in another, or rarely are seen only in one. Hence, a clinical diagnosis based on the underlying pathology should be attempted and may be helpful in governing prognosis and treatment.

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FAMILIAL AURICULAR FIBRILLATION*

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AURICULAR fibrillation is one of the commonest disorders of the cardiac mechanism, and its frequent occurrence in patients with otherwise normal hearts is now widely recognized. In spite of this, its familial incidence has been observed but rarely. The first recorded observation of this sort was made by Orgain, Wolff and White¹ in 1936. In 1942, Levy² reported the occurrence of paroxysmal auricular fibrillation and flutter without signs of organic cardiac disease in two brothers. The present paper records in detail the findings in three brothers with auricular fibrillation, mentioned briefly in the earlier report,¹ as well as 2 new cases of auricular fibrillation in brothers.

CASE REPORTS

CASE 1. H.K., a 25-year-old real-estate agent, presented himself for examination in 1927 for the purpose of having his heart "straightened out," so that the extra premium he was paying for life insurance might be removed. His mother and father, as well as two brothers (Cases 2 and 3), were alive and well. His mother was said to have had rheumatic fever. There was a possible history of diphtheria in childhood, mild influenza in 1918 and occasional sore throats prior to tonsillectomy in 1921. Frequent nosebleeds had occurred in childhood. Four to five years previously, the patient suffered from back pain, for which no cause could be found.

At birth, the attending physician thought the heart was irregular. From the age of seven through childhood he had always had a grossly irregular pulse. The diagnosis of auricular fibrillation was made for the first time when he was 20 years old, and a course of quinidine therapy at that time failed to abolish the abnormal rhythm. He lived an active, unrestricted life, and had palpitation only when excited. Although he was nervous and had fainted several times, he felt perfectly well and was apparently in excellent health. He smoked twenty cigarettes every day and drank occasionally, sometimes to excess.

Physical examination showed a well-built, healthy-looking young man. The only abnormality was the presence of a grossly irregular heart and a slight, inconstant apical systolic murmur. The apical rate was 80 per minute and was uninfluenced by exercise. The blood pressure was 110/70. The electrocardiogram was normal except for auricular fibrillation. After complete digitalization, quinidine sulfate restored normal rhythm. An electrocardiogram taken within an hour showed a PR interval of 0.16 second and digitalis T waves.

One and a half years later, after a drinking bout, auricular fibrillation recurred. Quinidine alone failed to restore normal rhythm. The patient was therefore digitalized. Quinidine then abolished the abnormal rhythm.

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He remained well for 2½ years, when another drinking bout was followed by the occurrence of auricular fibrillation. Again digitalis and quinidine restored the normal cardiac mechanism. Another recurrence of auricular fibrillation, without obvious cause, took place 1½ years later. Although digitalis and quinidine again restored normal rhythm, the rhythm became irregular within 2 months. After a short trial of quinidine therapy by the family physician without success, further treatment was refused. Up to the present time (February, 1943), the patient's health has remained excellent in spite of persistent auricular fibrillation. Digitalis has not been required.

CASE 2. V.K., a 31-year-old businessman, presented himself for examination in March, 1928, for treatment of a cardiac condition that he believed similar to that of his brother (Case 1). He had had measles, diphtheria, pertussis, mumps and tonsillitis in childhood. At the age of 8, he had pains in the legs, but was not disabled. The tonsils and adenoids were removed when he was 13 years old. In 1917, he had influenzal pneumonia and was in bed for 2 weeks. He smoked thirty cigarettes daily, but used very little alcohol, coffee or tea. As far back as he could remember, he had been very nervous and had had a quick temper. During the last 4 years his responsibilities had greatly increased, and he had had several fainting spells during this period.

The heart had been irregular since early childhood, but a diagnosis of auricular fibrillation had been made for the first time 7 months before the present examination. The patient played tennis and baseball and was very active generally. His only complaint was palpitation under great excitement.

Physical examination showed a well-developed, fairly well-nourished man. The heart rhythm was absolutely irregular at a rate of 76 per minute, which corresponded with the pulse rate. The sounds were of good quality and there were no murmurs. The blood pressure was 108/80. Electrocardiographic tracings showed auricular fibrillation with a ventricular rate of 70. There were no other abnormalities. After complete digitalization, quinidine caused a reversion to normal rhythm. Electrocardiograms then showed a PR interval of 0.20 second and digitalis T waves. Examination of the heart revealed no abnormalities except for a systolic murmur that was audible at the apex and pulmonic area but disappeared completely on full inspiration. Two days later the PR interval was 0.16 second.

When the patient was last seen, 20 months after the first examination, normal rhythm was still maintained. He had been living his usual active life, smoking as much as ever and occasionally drinking, without any harmful effects.

CASE 3. M.K., a 24-year-old law student, was first seen in June, 1928, at the request of his two brothers (Cases 1 and 2). During childhood he had had measles, an occasional cold and rarely a sore throat. For several years, when tired, he had had generalized, steady, dull pains in

the legs. At the age of 9, herniotomy and tonsillectomy were performed, and at the age of 15 the appendix was removed. The patient smoked twenty to twenty-five cigarettes every day, and drank two or three cups of coffee and one cup of tea daily and alcohol irregularly.

At the age of 14, he was told that his heart was irregular and was advised to avoid strenuous exertion. Nevertheless he played tennis, baseball, football and hockey and could swim 3 miles without untoward symptoms. He had palpitation only when excited. Nervousness was always marked and fainting or dizziness occasionally occurred.

Physical examination revealed a tall, fairly well nourished young man. There were no abnormalities except for an absolutely irregular cardiac rhythm. The apex and pulse rates were 80 per minute. The blood pressure was 118/80. Electrocardiograms were normal except for auricular fibrillation, the ventricular rate was 70. After complete digitalization, quinidine restored normal rhythm. Electrocardiograms taken immediately after the change in rhythm showed a PR interval of 0.20 second and digitalis T waves.

The patient was seen for the last time 2 months after the first examination. Normal rhythm was still maintained.

CASE 4 S O S, a 35-year-old physical director was first seen in April, 1928. The chief complaint was palpitation of 10 years' duration. The past history was negative except for Neisserian infection 17 years previously, mild influenza in 1918 and psoriasis 1 year previously.

His general health had always been excellent except for attacks of palpitation, which occurred about once a week and lasted half an hour and were apparently related to excitement, exertion or the drinking of whiskey. During the attacks, he was conscious of rapid and irregular heart action. Although he felt weak, he continued whatever activity he was engaged in. Less frequent attacks of a different type of palpitation occurred in which the heart beat much more rapidly and was regular except for occasional intermittence. They were stopped by bending forward. The patient's activities consisted of wrestling, boxing, swimming and road work. He could run 10 miles without untoward symptoms. He was nervous and introspective.

Physical examination disclosed a well-developed and well-nourished muscular, healthy athlete. The heart was normal, but the first apical sound was reduplicated. The blood pressure was 104/70. The tip of the spleen was just palpable. Roentgenographic measurements of the heart were within normal limits. The blood Wassermann reaction was negative. Electrocardiograms were obtained during paroxysms of auricular fibrillation as well as during normal rhythm.*

Seven years later (1935), after untreated persistent auricular fibrillation for 6 months, the patient was examined at another clinic,⁴ where congestive failure and moderate cardiac enlargement were found. Following digitalization, quinidine restored normal rhythm. Improvement was striking and for the next 5 years he was able to carry on well. There was an occasional paroxysm of auricular fibrillation. In 1939, the transverse diameter of the heart was 14.8 cm, compared to 14.1 cm in 1928.

CASE 5 S S, the 25-year-old brother of the patient in Case 4 entered the Beth Israel Hospital in March 1931,

complaining of attacks of palpitation of 2 years' duration. In childhood he had had diphtheria, measles, scarlet fever and frequent sore throats. He drank whiskey and beer occasionally and two or three cups of coffee daily, he did not use tobacco.

During the last 2 years he had had several attacks of palpitation lasting as long as 36 hours. Ten months before admission, after exercising in a gymnasium, he had an attack accompanied by constricting precordial pain. Examination showed auricular fibrillation and spontaneous pneumothorax (x-ray). Following this he had palpitation and dyspnea, especially at night, but continued working strenuously as a warehouseman and played basketball and other games. He was nervous and introspective.

Examination revealed no abnormal findings except auricular fibrillation, with an apical rate of 90 per minute. The blood pressure was 122/80. The basal metabolic rate was +10 per cent. Electrocardiograms showed a tendency to right axis deviation, auricular fibrillation with a ventricular rate of 100 and normal T waves and RST segments. After reversion to sinus rhythm, normal P waves and PR intervals were present. A roentgenogram of the chest revealed slight scarring of the left apex and emphysema. After complete digitalization, quinidine restored normal rhythm.

During the succeeding 8 years, paroxysms of auricular fibrillation have recurred occasionally, but the patient's general health has remained good. At present there is no evidence of structural heart disease.⁵

DISCUSSION

The great frequency and ease of recognition of auricular fibrillation warrant the conclusion that the familial occurrence of this arrhythmia is rare. Indeed, the two sets of brothers here reported are unique in medical literature, in the cases reported by Levy,² one brother had auricular fibrillation, the other auricular flutter. This is in marked contrast to other common disorders of the heart such as rheumatic, hypertensive and coronary heart disease, in which it is not unusual for several cases to occur in a single family.

There are several noteworthy features in the first set of brothers (Cases 1, 2 and 3). One of them had frequent nosebleeds, the other two growing pains in childhood. During the fetal life of M K (Case 3), his mother is said to have had rheumatic fever. All three brothers had permanent auricular fibrillation, in contrast to paroxysmal fibrillation in the remaining cases in a series with normal hearts previously reported.¹ An arrhythmia was constantly present years before a diagnosis of auricular fibrillation was made, suggesting that an abnormal mechanism was present at birth or developed early in life. Congenital auricular fibrillation is suggested, particularly in Case 1. The three brothers lived normal, unrestricted lives and two of them engaged in strenuous sports without difficulty of any sort. Although the ar-

*A more complete description of these electrocardiographic tracings may be found in a previous publication by Wolff, Parkman and Wilke.²

rhythmia was untreated, the ventricular rates were slow, even after exercise. Auriculoventricular conduction time, measured in each case immediately on resumption of sinus rhythm, was normal. It was thought that an unusually rapid auricular rate (circus movement) might be responsible for the slow ventricular rate, since it was possible to count 800 oscillations to the minute in the limb leads as well as in chest (CB) leads (Case 3). Notching of the auricular deflections, however, could have accounted for the apparently rapid rate. A more likely explanation for the slow ventricular rate was furnished by the evidence of strongly preponderant vagal tone, which also may have been a factor in the production of auricular fibrillation.⁶⁻¹⁰ With normal rhythm, each of the brothers had a very slow and irregular heart (sinus arrhythmia). Nervousness, low blood pressure, dizziness and fainting spells were also present. There was no evidence of thyrotoxicosis.

The benign nature of auricular fibrillation, provided that the ventricular rate is controlled and embolism does not occur, is illustrated by these cases. In spite of the abnormal rhythm of many years' duration, completely unrestricted activity was possible, even without the use of digitalis or other cardiac drugs. The heart size remained normal, and it was impossible to demonstrate any structural abnormality whatsoever.

Case 4 is of historical interest, being the first in which the combination of short PR interval, changes in QRS complexes resembling bundle-branch block and paroxysmal tachycardia was recognized as a distinct clinical entity.³ This mechanism was not demonstrable in the patient's brother (Case 5), but in other respects they were much alike. There was no evidence of thyrotoxicosis.

The value of the combined administration of digitalis and quinidine for abolishing auricular fibrillation, especially when quinidine alone is ineffective, is again demonstrated by these cases.¹¹

SUMMARY

Permanent auricular fibrillation in three brothers and paroxysmal fibrillation in two brothers, with otherwise normal hearts, have been reported. Familial auricular fibrillation is apparently rare, in contrast to certain other cardiac disorders that commonly occur in several members of a single family.

There is evidence of increased vagal tone in these cases, suggesting a probable etiologic factor in the production of auricular fibrillation in certain cases.

Auricular fibrillation, even when untreated and of many years' duration, is entirely benign, provided that the ventricular rate is slow and embolism does not occur. Under these conditions, auricular fibrillation does not cause cardiac enlargement.

The combined administration of digitalis and quinidine for abolishing auricular fibrillation was in these cases superior to the use of quinidine alone.

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ACUTE PNEUMONITIS AND PERICARDITIS*

Report of a Case

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BECAUSE of the widespread interest in the prevalent pulmonary infection known variously as pneumonitis, virus pneumonia or simply atypical pneumonia, the following clinical history is presented. We were particularly interested in interpreting the bizarre changes in the electrocardiograms of this patient as correlated with the clinical and x-ray findings. We have subsequently observed the same cardiographic changes, to a lesser degree, in certain other patients suffering from this condition, particularly since we now take routine tracings on all patients with respiratory infections who have temperatures of 100°F or over. In 11 out of 100 cases observed, an elevation of the ST segment of 2 mm above the isoelectric line (generally in Lead 4) was noted. In 5 additional cases there was inversion of the T wave in Lead 4. On recovery, all the variations returned to normal.

CASE REPORT

C J, a 36-year-old man, was admitted to the Medical Service of the United States Naval Hospital at Newport, Rhode Island, on July 8, 1942, complaining of pain in the interscapular region of 1 week's duration and of non-productive cough. The backache was sharp in character and grew worse on movement, breathing or coughing. There had been no chills. He had suffered from an upper respiratory infection (sore throat, fever and cough) 3 weeks previously. This had cleared except for a residual cough.

The past history revealed the occurrence of pleurisy at the age of 11. The family history was noncontributory.

Physical examination disclosed an acutely ill man, slightly cyanotic and somewhat dyspneic. Dullness was noted over the lower lobe of the right lung posteriorly, below the angle of the scapula. Slightly increased breath and voice sounds and coarse rales were heard. The left lung showed dullness at the base, with scattered rales. Percussion of the heart revealed possible enlargement. No murmurs or friction rub was heard. The blood pressure was 110/60. The temperature was 99.4°F, and the pulse 83.

The white cell count was 10,500, with 68 per cent neutrophils and 23 per cent lymphocytes. The sedimentation rate was increased. The antistreptolysin titer was nor-

mal. The sputum contained some gram positive diplococci, which could not be typed.

X-ray examination revealed an infiltration of both lower lung fields, especially the left, and enlargement of the

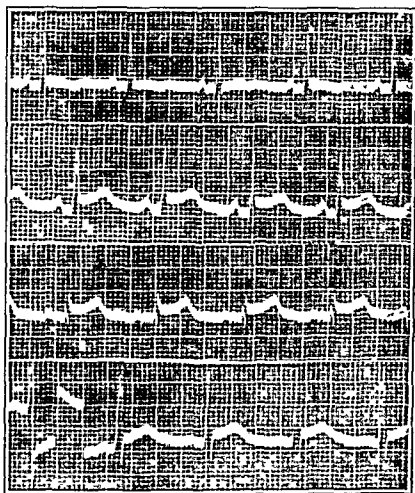


FIGURE 1 Electrocardiogram Taken on July 8

cardiac silhouette. An electrocardiogram presented an inverted T wave in Lead I and an elevated ST segment in Leads 2, 3 and 4 (Fig 1). On July 11, x-ray films showed recession of the process in the lower left chest but increased density in the lower part of the right lower lobe. On July 15, the T waves were inverted in Leads 1, 2 and 4, with coving (Fig 2), and x-ray examination showed clearing in the right lower lobe but involvement of the right middle lobe. On July 20 (about the 20th day after onset), the T waves were upright in all leads and the electrocardiogram had returned to normal (Fig 3).

The following day, the patient suffered a recurrence of pain between the shoulderblades and in the epigastrium. X-ray examination demonstrated an infiltrating lesion in the upper portion of the right lower lobe. The cardiac silhouette, however, had returned to normal size. An electrocardiogram on the following day revealed inverted T waves in Leads 1, 2 and 3 (Fig 4). The next x-ray examination, performed on July 28, again showed clearing in the right lower lobe but also demonstrated a new le-

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sion in the right middle lobe. Clinical findings, x-ray evidence and electrocardiographic changes remained the same until August 4, when the chest film showed considerable improvement. The T waves were still inverted in Leads 1 and 3, but by August 12 the tracing had returned to normal and remained so. On that date x-ray examination also showed complete resolution of the pneumonic processes. Sulfonamide therapy was of no avail during either the initial stage of the illness or the relapse.

At the time of first examination the problem appeared to lie in ruling out myocardial infarction. We finally decided for the reasons given below that not coronary occlusion but pericarditis was producing the alterations in the electrocar-

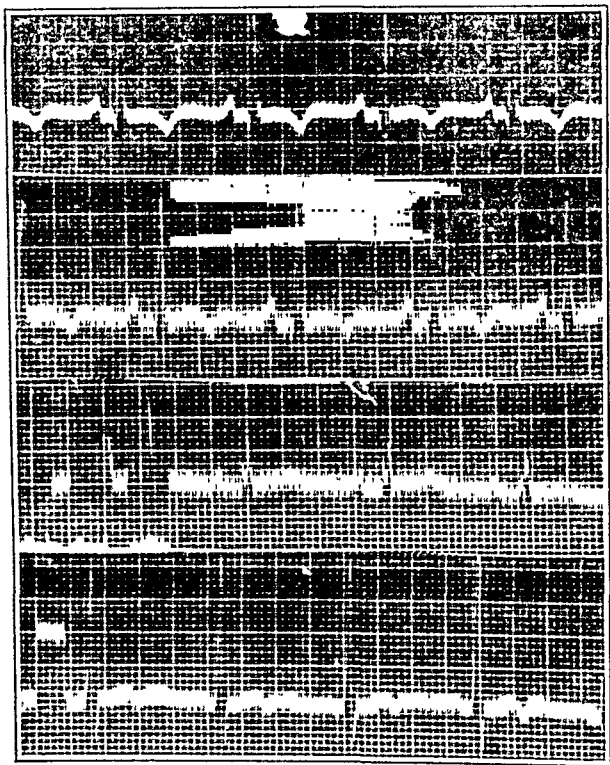


FIGURE 2. *Electrocardiogram Taken on July 15.*

diographic pattern. Early in the differential study dissecting aneurysm was considered, because of the location of the pain, but this possibility was dismissed for want of evidence and because of the manifestations of pulmonary and cardiac changes. Acute mediastinitis was discussed, but Commander E. F. Merrill, roentgenologist at the hospital, did not think that the x-ray evidence supported this possibility. Fiedler's interstitial myocarditis was given but slight consideration. Although this condition may produce somewhat similar electrocardiographic changes and initially may resemble the clinical picture as presented, the return of the heart to normal size and the complete recovery of the patient eliminated this possibility.

The next problem was concerned with the pulmonary changes. It was thought that the rapid

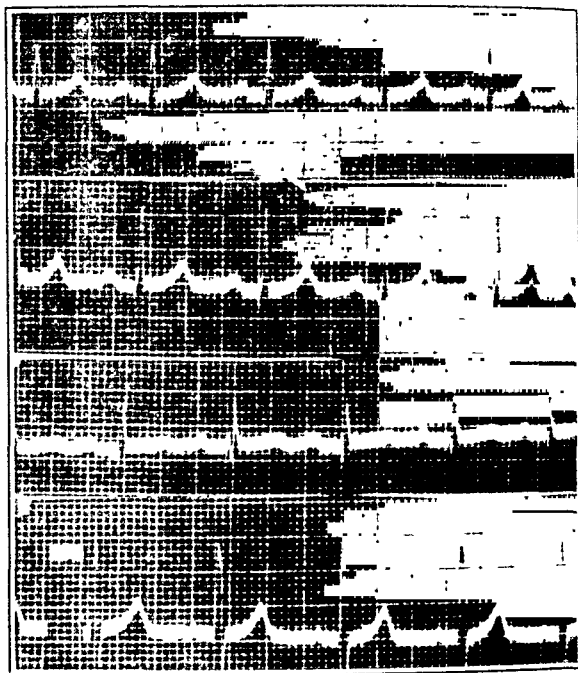


FIGURE 3. *Electrocardiogram Taken on July 20.*

ity of clearing of the pulmonary fields and the lack of residual alterations eliminated multiple pulmonary infarctions as the source of the lesions. Rheu-

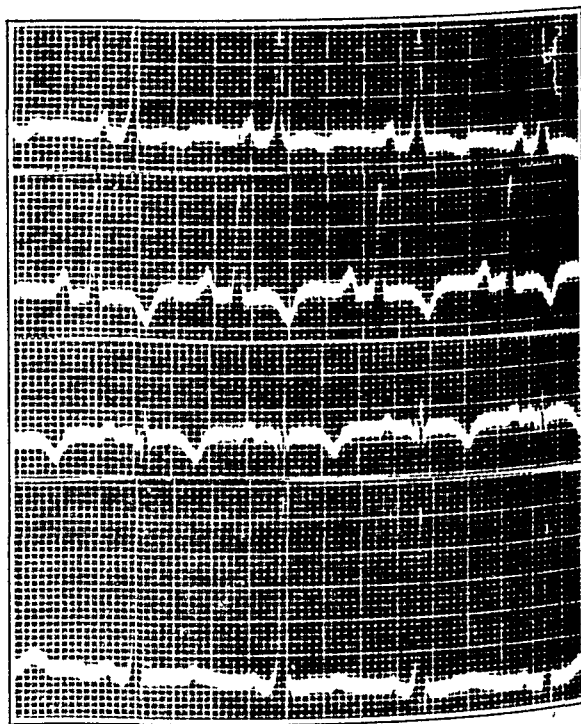


FIGURE 4. *Electrocardiogram Taken on July 22.*

matic fever with rheumatic pulmonary changes and pericarditis might produce the picture de-

scribed. However, at no time did the patient manifest joint involvement and he never exhibited any signs of congestive failure, a finding that is frequently observed with so-called "rheumatic pneumonitis." It is true that the sedimentation rate was increased, but this would be expected in the presence of any acute pulmonary infection. The antistreptolysin titer was normal, however, and we have found this to be uniformly elevated during acute rheumatic fever, especially during the first attack. Following the subsidence of the pericarditis no other evidence of acute rheumatic fever with rheumatic heart disease was found. On the basis of these facts we eliminated this entity in favor of one that consistently manifested x-ray changes similar to those described in this case. In addition, subsequent study produced similar though less marked cardiographic changes in about 15 per cent of the patients with these x-ray changes.

DISCUSSION

This patient displayed five distinct areas of pneumonia during the course of his illness, and it will be noted on following the clinical progress that the variations from and return to normal in the electrocardiograms corresponded closely to the pulmonary changes. These variations consisted in elevation of the ST segment and T wave inversion, frequently with coving. The alterations were in the same direction with regard to the base line in various leads in contrast to the changes in myocardial infarction, which are reciprocal, that is, in infarction due to acute anterior coronary occlusion the ST segments may be elevated in Leads 1, 2 and 4 but are depressed in Lead 3. In addition, no Q wave was noted and there was no disappearance of the R wave in Lead 4, as in anterior infarction. In posterior infarction the ST segment is elevated in Leads 2 and 3 but not in Lead 1, where a depression of this segment may be found. The absence of a prominent Q wave in Leads 2 and 3 also helped to differentiate this condition and posterior infarction. Finally, the pattern changed too rapidly and returned to normal too quickly to correspond with that due to infarction.

The changes were in accord with those found in acute pericarditis. They have been described by many investigators and are believed to be due, not to tamponade of the heart, but to acute subepicardial myocarditis. They are characteristically evanescent and may last only a few days, since the

changes are not due to the death of the myocardial tissue but to inflammation. It should be stressed at this point that at no time were any physical signs of pericarditis evidenced—a strong recommendation for the use of the electrocardiogram in similar respiratory infections. The literature shows that the use of Lead 4R is preferable to that of Lead 4F when this condition is suspected, although we used Lead 4F in this study.

One other state should be mentioned as a possible causative factor in the production of the abnormalities, particularly the less marked ones, observed in the tracings of our series. This is hyperventilation, which is known to produce transient electrocardiographic changes. We do not believe that the marked changes produced in the case reported can be accounted for by this phenomenon, but have not investigated it in the other cases with minor changes.

There are three electrocardiographic patterns to be kept in mind as being important from the point of view of differential diagnosis. First of all, a patient who has had a previous pattern of myocardial strain with a superimposed coronary thrombosis may show bizarre tracings similar to those described in this case. Secondly, one must take care to exclude an infarct complicated by bundle branch block. Thirdly, one must rule out a combined anterior and posterior infarction. The absence of a Q pattern aids in this regard, and in addition the study of serial tracings for evidence of a changing pattern as well as observation of the time interval before the pattern returns to normal, is all important.

SUMMARY AND CONCLUSIONS

A case of acute pneumonitis with bizarre electrocardiographic findings, presumably due to acute pericarditis, is reported.

It seems advisable to take electrocardiograms in severe cases of acute atypical pulmonary infection. In this way, acute pericarditis may be diagnosed in the absence of physical signs or before the latter appear, and the tracing may aid in accounting for prolongation of illness or unexplained symptoms and signs. Secondly, one should beware of diagnosing coronary occlusion too readily. Serial tracings should be made, and alterations in pattern should be observed, as well as the time interval, before the return to normal occurs.

MEDICAL PROGRESS

BRIGHT'S DISEASES (Concluded)*

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Intercapillary Glomerulosclerosis

THE description by Kimmelstiel and Wilson⁵¹ in 1936 of a severe nephrotic syndrome associated with hypertension and uremia, complicating the course of diabetes mellitus and apparently attributable to a sclerotic lesion between the capillaries of the glomerular tuft that they called "intercapillary glomerulosclerosis," has resulted in a reconsideration of pathologic material in many laboratories and in the clinical segregation of such cases in many diabetic clinics where previously they had been overlooked. This movement has continued during the past year with the appearance of case reports and reviews of necropsy material. Horn and Smetana⁵² at Columbia University re-examined diabetic and arterial nephrosclerotic autopsy material and found typical lesions of intercapillary glomerulosclerosis in 22.9 per cent of the diabetic and 25.4 per cent of the nephrosclerotic kidneys, figures that are in striking contrast to those of Siegal and Allen⁵³ of 33.3 per cent and 1.0 per cent, respectively. The lesions were always associated with arteriosclerosis, and it is noteworthy that the severer lesions were always associated with diabetes mellitus. Bell⁵⁴ in Minneapolis has reviewed the kidneys of 460 persons with diabetes, finding hypertension more frequent among them than in the population at large, and finding intercapillary glomerulosclerosis in 20.5 per cent of the diabetic patients. Hyaline masses between the glomerular capillaries, apparently attributable to splitting and thickening of the basement membrane, along with hyalinization of the afferent and efferent arterioles, were the outstanding pathological findings. Horn and Smetana, as well as Bell, stress the nonspecificity of the lesions, which apparently cannot be made the basis of a pathological diagnosis of diabetes mellitus.

Amyloid Nephrosis

During recent years Hass⁵⁵⁻⁵⁷ at Cornell has conducted a study of the nature of the substance deposited throughout the body in amyloid dis-

ease. He has succeeded in separating two protein fractions and a sulfate-bearing polysaccharide from amyloid found in the liver, spleen and other organs. Amyloid from all these sites has common chemical and tinctorial features, although three distinct types of amyloid are identifiable. All are protein-protein complexes and Hass subscribes to the view that all are derived from the deposit and alteration of antibody-antigen combinations. This view is widely held because amyloid deposits appear almost always in conditions where the immune mechanisms have been exposed to prolonged stimulation, as in chronic pyogenic or tuberculous infections. They are easily produced in animals by pyogenic sepsis, especially on the basis of invasion by staphylococci, and by toxins, especially diphtheria toxin when used for the production of immune serum. The appearance of amyloid in such conditions as chronic diffuse glomerulonephritis and multiple myeloma seems to weaken this explanation, but in the first, long-standing occult infections may be at fault, and in the latter the hyperglobulinemia may indicate some connection with the immune mechanisms. The polysaccharide recently isolated by Hass cannot be distinguished chemically from chondroitin-sulfuric acid found in cartilage or from heparin. This gross chemical resemblance to heparin is of interest from the standpoint of pathology, for the lesions are almost invariably found beneath the endothelium of vessel walls. The fact that in vitro production of amyloid with antigen and antibody is not possible is no deterrent to acceptance of the theory, for, as Hass has pointed out, the formation of amyloid is slow and time consuming. Since Congo red, not a unique substance, can easily change the character of amyloid, Hass concludes that many other substances with similar properties are present in the blood and alter the antigen-antibody complex in vivo in a manner that cannot be duplicated in vitro. However, this explanation fails to throw light on the mechanism of the ready and rapid removal of the substance following elimination of the causative focus of infection in many cases. In addition, Snapper⁵⁸ notes the extremely low incidence of amyloidosis in China, where 1.3 per cent of the cases of chronic

The articles in the medical progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas, 1942. \$5 00).

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tuberculosis are complicated by the disorder in contrast to varying estimates of 22 to 25 per cent in this country.^{58, 59} Snapper stresses the apparent importance of a milk-free and casein-free diet in determining the low incidence of amyloid disease in northern China.

Considerable interest has been shown during the past year in the refinement and quantitation of the Congo red test. Harmon and Kernwein⁶⁰ suggest the use of 4 mg. per kilogram of body weight, taking blood samples at the usual four-minute and sixty-minute intervals after injection, but Taran and Eckstein,⁵⁹ at the Sea View Hospital, Staten Island, New York, point out that Congo red may be removed so rapidly following administration that a sample taken four minutes later will give a falsely low standard, and they suggest shortening this interval to two minutes.

Benign Proteinuria

The appearance of protein in the urine is usually evidence of an underlying renal disorder of a serious character and may include any of the Bright's diseases. However, cases of proteinuria in the absence of demonstrable renal disease include benign albuminuria, orthostatic albuminuria and the larval nephroses, and may be considered arbitrarily as nephroses. The importance of orthostatic albuminuria today in its relation to military medicine has recently been emphasized by Young and his associates,⁶¹ who report 4 cases of men rejected for military service by medical examining boards because of persistent albuminuria. Extensive studies revealed no renal disease, and it was found that the albuminuria appeared only in the erect posture. These men were then accepted for service. Young emphasizes the benignity of the condition and reviews the cases seen at the Johns Hopkins Hospital. In 67 cases, 4 (6 per cent) proved on follow-up to have chronic nephritis. This incidence, however, is high enough to warrant close follow-ups in all cases and should indicate a somewhat less optimistic outlook, although, of course, coincidence cannot be ruled out as a factor in this small series.

Transient proteinuria (larval nephrosis) frequently appears in the course of acute infectious diseases and febrile states. The usual pathological findings include cloudy swelling of the tubular cells and hyaline-droplet degeneration. Kannerstein⁶² reviewed the renal lesions found at death in the midst of various acute infectious diseases and found tubular changes most marked in diphtheria, where epithelial necrosis appeared in 16 per cent of cases. Interstitial infiltration appeared in 48 per cent of cases of diphtheria and in 77 per cent

of cases of scarlet fever, representing an inflammatory reaction or nephritis that would have been impossible to diagnose clinically.

Therapy of Nephrotic Edema

In most of the nephroses mentioned thus far the management of edema is the outstanding therapeutic problem. Rational therapy must be directed at replacing the lost intravascular protein or at furnishing a substitute with similar properties in order to re-establish normal osmotic relations. To this end, extensive therapeutic programs with the use of transfusions of plasma and serum or concentrates of plasma and serum have been conducted. In many respects this approach has proved disappointing, as is exemplified by the studies in England of Brown, Gray and Mollison⁶³ appearing during the past year. These workers found that concentrated serum and plasma transfusions were not followed in most cases by increased plasma protein and in fact seemed as likely to be followed by adverse effects as by good effects, results confirming several earlier studies in this country. The use of acacia as a substitute for the lost plasma proteins has found support in the United States, particularly at the Mayo Clinic, where acacia has been given an extensive therapeutic trial. During the past year Lehnhoff and Binger⁶⁴ have added 12 more cases of nephrosis treated effectively with acacia to the series already reported from the Mayo Clinic. They find the substance efficacious in relieving the edema of nephrosis and believe that it is safe. However, there is experimental proof that acacia is stored in the liver, to remain there for long periods of time.⁶⁵ Heckel, Erickson, Yuile and Knutti⁶⁶ showed a reduction in plasma proteins after administration of acacia that could not be entirely accounted for by the increase in plasma volume, apparently indicating liver damage with impaired hepatic regeneration of protein. Farr⁴⁹ thinks that the use of acacia is not justifiable since other substances (concentrated human plasma and serum) are available that behave in exactly the same manner and are not dangerous. Obviously, every effort must be made to build up the plasma protein by increasing protein intake. In addition, of course, sodium deprivation is mandatory in preventing to some extent further accumulation of edema fluid.

The diuretics seem to be useful in controlling the edema in many nephrotic patients. Ammonium chloride and the potassium salts are in wide use. Farr⁴⁹ recommends urea in doses of 45 to 60 gm. daily because it is effective and seems to be harmless. The mercurial diuretics have not been proved detrimental to the kidney and are

very effective in establishing diuresis. However, the dangers of their use have received much attention during the past year, and editorial warnings have been sounded in the *Journal of the American Medical Association*⁶⁷ and in the *Lancet*.⁶⁸ These warnings have been addressed to the profession because of the appearance of case reports of sudden death following the administration of mercurial diuretics. DeGraff and Nadler⁶⁹ point out that the usual type of toxic response is attributable to the dehydrating action with chloride loss, resulting in a shock-like state. However, by far the most dangerous type is apparently attributable to ventricular fibrillation due to the direct action of mercury on the heart. In all, some 26 fatal cases have been reported, a number that is infinitesimal in comparison with the millions of injections that have been given.

Mercurial Nephroses

Mercury produces a specific lesion in the renal tubules characterized by necrobiosis, necrosis with sloughing of the epithelial cells into the lumen of the tubule, collapse and rupture of the tubules, and frequently calcification of the necrotic lesions. The lesion is typical in many respects of those seen in the second group of nephroses described above, the necrotizing nephroses. Mercury appears to exert its main effect on the midportion of the proximal tubular segment, rarely with injury to portions of the distal segment and thin segment.⁷⁰ The finding of Holman and Donnelly⁷¹ that hypoproteinemia appears to protect the kidney in dogs may explain the infrequent occurrence of renal damage in nephrotic patients treated extensively with mercurial diuretics.

Sulfonamide Nephrosis

Like mercury, the sulfonamides have proved dangerously nephrotoxic. Numerous reports of cases of renal damage during the course of sulfonamide therapy have continued to appear in the literature during the past year. The renal damage has been attributed to the blocking effect of crystals of the free and acetylated drug. This explanation has much to recommend it in the majority of reported cases, for dilatation of the tubules and the malpighian corpuscles anterior to the blocking crystals is frequently seen. In addition, tubular necroses are often observed, and lesions similar to those seen in the crush syndrome have been reported on several occasions. In these cases a hemolytic anemia due to the drug appears to be the most important underlying factor.⁷² It is worth remarking that these drugs are relatively safe in the presence of uremia resulting from in-

trinsic renal disease. Fishberg,⁷³ for example, describes the successful use of sulfonamide in the treatment of lobar pneumonia appearing in the course of chronic pyelonephritis associated with renal insufficiency and azotemia. This may be ascribed to the low specific gravity of the urine and to the fact that the kidney does not concentrate the drug within the tubular urine at dangerous levels. Small doses of the drug, however, are required to maintain high blood levels in these patients. It is interesting that the sulfonamides appear to become more soluble as urinary concentration increases, owing to the fact that high concentrations of urea render the drugs more soluble.⁷⁴ This finding may have therapeutic bearing in supporting the use of urea during the administration of the drug for its action of inducing diuresis and increasing sulfonamide solubility, as well as for whatever bacteriostatic effect it may have. It cannot be emphasized too frequently that adequate hydration and alkalization are of paramount importance in preventing renal damage by the sulfonamides.

The Crush Syndrome and Related Conditions

During the past year the so-called "crush syndrome" has continued to excite considerable interest⁷⁵ and has stimulated numerous efforts to solve its etiology and pathologic physiology. It is becoming increasingly apparent that an important group of renal disorders, nephrotic in type, is achieving homogeneity as a result of these studies. These nephroses include the renal lesions seen following intravascular hemolysis during malaria (blackwater fever) or after the administration of incompatible blood and those seen during myohemoglobinemia and hemolytic anemia due to sulfonamide, as well as those of the crush syndrome. In all these conditions there are numerous casts in the urine, the collecting ducts and the distal tubules, along with necrotic changes in the tubular cells. In all of them the *sine qua non* in the cycle of events leading to uremia seems to be the extracellular appearance of hemoglobin or other heme-bearing pigment in the circulating blood.

Bywaters and his colleagues⁷⁶⁻⁷⁸ have reported cases of renal insufficiency following crushing injuries seen during the heavy bombing of London in the fall of 1940 as examples of a new syndrome, for they were unaware of similar cases reported in the German literature following World War I. These patients had usually been pinned by the extremities beneath heavy beams or other debris for several hours. Following release they usually

appeared well save for complaints referable to fractures, lacerations and other injuries. The compressed limb was pale, cold and pulseless, with evidence of some motor and sensory loss. Following rescue, tense swelling of the limb appeared and shock became evident with pallor, sweating, hemoconcentration and finally marked hypotension. (Duncan and Blalock⁷⁰ have shown experimentally that the shock is attributable to plasma loss into the tissue at the site of compression where capillary walls are damaged.) The swelling of the limb continued, but shock responded well in most cases to the intravenous administration of fluids and blood. Following recovery from shock the patients seemed well, but the urine was found to appear bloody, to contain albumin, creatine and pigmented granular casts, and to be highly acid. During the next few days the urinary output was as a rule very scanty, but the pigment usually disappeared after the second day. Despite the oliguria, the urine remained dilute. Often the condition of the limb aroused concern, and occasionally amputation in the presence of gangrene was performed. During the first week the blood pressure gradually rose to hypertensive levels, vomiting became a prominent feature, and the blood urea, phosphate and potassium levels gradually rose whereas the carbon dioxide combining power fell. At about the end of the first week, a critical diuresis followed by complete recovery occurred or, more frequently, urine flow ceased altogether and the patient died suddenly after two or three more days in uremia. At autopsy the kidneys were found to be engorged and swollen, with striking changes in the distal segment of the renal tubules ranging from cloudy degeneration to frank necrosis. The distal tubules and collecting ducts were jammed with brown granular casts, which were occasionally extruded into the interstitial tissue through the necrotic tubular wall. The muscular tissue at the site of injury was usually also necrotic and markedly pale. Bywaters⁸⁰ has emphasized the importance of the condition in modern warfare, since the bombing of urban centers is peculiarly adapted to the production of crushing injuries caused by the collapse of shelters, dwellings or other heavy construction. In an air raid as many as 5 per cent of the casualties may be of this type. More than 70 cases had been reported to the Medical Research Council in England by December, 1942.

When first observed, these cases were thought to be examples of transfusion reactions, but it soon became apparent that the syndrome was seen when transfusions had not been administered and

that it appeared only in patients with a history of compression injury. However, Bywaters and his colleagues⁸¹ were struck by the evidence of muscular damage,—namely, the muscular pallor and the creatinuria,—and they believed that a toxic substance, probably myohemoglobin, was released from the muscle. This hypothesis found support in the identification of the pigment in the urine.⁸² Bywaters⁸⁰ next attempted the experimental production of the renal lesion, and claimed success in producing it in the acidotic rabbit following the intravenous injection of myohemoglobin. However, Bing⁸³ was unable to confirm Bywaters's results, since in his experiments myohemoglobin proved harmless in the acidified dog. He suggested that Bywaters's effects might be attributable to the use of foreign protein, since the myohemoglobin used by Bywaters was obtained from some species other than the rabbit, which has no myohemoglobin in its muscular tissue.

Myohemoglobinuria occurs in man, however, under other circumstances, and there it is associated with renal insufficiency, a fact further bolstering Bywaters's hypothesis. Bywaters and Dible⁸⁴ have reported during recent months the eighth case of paroxysmal myohemoglobinuria to have appeared in man. This condition is seen as a rule in horses, where it is a serious complication of sudden exercise after rest or after heavy feeding and is apparently due to muscular loss of myohemoglobin. The affected muscles become stiff and paralyzed, and death occurs in uremia, in 20 to 70 per cent of cases with evidence of sepsis at the end of the first week. Lesions in the kidney resemble those of the crush syndrome.

On the other hand, renal disorders are known that resemble the crush syndrome in every respect but that do not require myohemoglobinemia for their genesis. The so-called "transfusion kidney" and the renal lesions in blackwater fever are striking examples. In such cases, too, a heme-bearing pigment, hemoglobin, is freed in the blood, and renal insufficiency is usually attributed to blockage of the tubules by the casts owing to the relative insolubility of hemoglobin in an acid urine. Since blocking of this sort is seen in the kidney of the crush syndrome and in myohemoglobinuria, a similar explanation has been evoked to account for the failure of kidney function in these disorders. In this view, the released pigment—whether hemoglobin or myohemoglobin—passes through the glomerular membrane and under conditions of acidosis is precipitated in the tubular urine, to form casts that block the further secretion of urine. A number of cogent arguments against

this hypothesis have, however, appeared during the past year. Ayer and Gauld⁸⁵ have pointed out that an identical pathologic picture is seen in the kidneys of severely jaundiced infants with congenital atresia of the bile duct in the absence of any sign of renal insufficiency. In addition, the blockage hypothesis implies some dilatation of the tubules and glomeruli proximal to the point of block, as is seen in obstruction by crystals of the sulfonamides. This is never seen in the renal lesion of the crush syndrome and of the transfusion reaction.⁷² Bywaters⁸⁰ has noted that the scant urine was dilute in all his cases, contrary to one's expectation if mechanical obstruction were to account for the oliguria. Thus it seems that the idea of cast obstruction as the primary cause for the oliguria and renal failure in these conditions must be doubted. In fact, cast formation may be regarded as a phenomenon secondary to a markedly reduced glomerular filtration rate.^{72, 83}

Whatever the mechanism by which renal failure is brought about, it seems likely that it is common to all these nephroses and that a substance toxic to tubular cells and interfering with renal hemodynamics is involved. It also seems clear that this hypothetical substance is derived from or through the agency of the heme-bearing pigment, for the pathologic picture is always seen when a heme-bearing pigment is at large in the blood and may be seen—in transfusion reactions, for example—in cases in which no tissue damage is apparent as a source of a toxic agent. Curiously enough, the heme-bearing pigments do not seem to be nephrotoxic in normal animals and in man. However, renal tubular lesions have followed the intravenous injection of heterologous myohemoglobin in the acidified rabbit⁸⁰ and of homologous methemoglobin in the acidified dog.⁸³ Ferrihemic acid, a breakdown product derived from methemoglobin, has also been used successfully to produce tubular damage in the dog.⁸⁶ Anderson, Morrison and Williams,^{80, 87} who claim that this substance, derived from the pigment of the malarial parasites, is responsible for the kidney lesion of blackwater fever, have expressed the opinion that it acts indirectly through vascular injury and thrombosis rather than directly on the tubular cells. There is much evidence, however, that the tubular cells are directly affected in all these nephroses. Anatomically, there is marked disorganization of the structure of these cells, especially those of the distal segment, and physiologically certain tubular functions, largely carried out in the distal segment, are gravely disturbed. It is noteworthy that acidemia, a prominent clinical feature, is necessary before the lesions can

be produced experimentally. In addition, the urine remains highly acid, despite efforts to alkalinize it, both in man and experimental animals, once the condition has been established.⁷² These facts suggest that the distal segment function of acidification may be involved in some fashion in the initiation and perpetuation of the renal lesion. The ability of the kidney to concentrate the glomerular filtrate, another distal segment activity, is also seriously interfered with, for the urine remains dilute despite the oliguria. Furthermore, there is evidence that the glomerular filtration rate and the renal blood flow are markedly reduced.^{72, 83}

Therapy in these disorders remains largely empirical. Since the scanty flow of urine has heretofore been attributed to blockage by casts of precipitated pigment, it has seemed reasonable to increase water intake as a measure directed to washing out the casts and to alkalinize the urine in order to increase their solubility. In the light of the more recent work, the rationale of this therapy appears to be seriously weakened. It has, however, proved effective in practice, and until better methods based on more complete knowledge are developed, alkalinization and hydration will doubtless remain the procedures of choice. Bywaters⁸⁰ has emphasized the value of forcing fluids and of alkalinization in preventing renal insufficiency following compression injuries, and Smith and Evans⁸⁸ give enthusiastic support to these measures in blackwater fever. It is conceivable that hydration is of value because it may increase the decreased filtration rate, but no good evidence that alkaline therapy is beneficial has been adduced. Indeed, it is possible that alkalinization may be harmful,⁷² although this point is highly controversial and awaits further experimental elucidation. Duncan and Blalock⁷⁹ have shown the efficacy of pressure in preventing local loss of fluid following crush injury, and this principle has found clinical application in the hands of Patey and Robertson,⁸⁹ who advocate elastic bandaging of the crushed extremity to prevent shock and the rapid return of toxic substances to the general circuit.

Bilateral Cortical Necrosis

In 1941, Duff and More⁹⁰ reviewed 71 cases of bilateral cortical necrosis reported in the literature and surveyed the experimental work on this subject. The disorder had been observed in 48 pregnant women and in 8 nonpregnant women and in 15 males from thirteen to sixty-four years of age. The necrotic lesions in the renal cortex had appeared in varying degree after a variety

of conditions. There seems to be common agreement that a toxic factor is to blame, and Duff and More believe that the actual effects in the vessels of the renal cortex vary with the degree of hypersensitivity of the vessels and with the intensity and duration of action of the toxic factor, stasis, thrombosis and marked vasoconstriction of the arteries of the renal cortex all playing more or less important roles. In the past year Sheldon and Hertig,⁶¹ at the Boston Lying-in Hospital, have reported 2 cases that are typical in most respects of the clinical and pathologic picture. In each the disorder was observed following abruptio placentae and was characterized clinically by oliguria and anuria, with rapid progression to a fatal termination in uremia. The kidneys were increased in size, with multiple areas of necrosis in the cortical zone. The fundamental lesion consisted of degeneration in the wall of the afferent arteriole at the point of entry into the glomerular tuft, as associated with local thrombosis and retrograde extension, resulting in multiple local infarction. Areas of necrosis were also found in other organs, and Sheldon and Hertig were impressed by the appearance of necrotic lesions in the anterior lobe of the pituitary gland in their cases, a finding that led them to believe that the condition was associated in some obscure manner with the endocrinal reorganization in pregnancy. Similar lesions have been produced experimentally in animals by many different methods, and in the past year Christensen⁶² has found that cortical necrosis appears in white rats fed low choline or choline-deficient diets.

The specific toxemia of pregnancy is usually considered to be a nephrosis complicated by hypertension that appears in the course of pregnancy, possibly on a congenital hypertensive background. Advances in this field have recently been discussed by Reid⁶³ in this series of medical progress reports and will not be further considered here.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 29351

PRESENTATION OF CASE

First admission. A forty-two-year-old American salesman entered the hospital because of shortness of breath of one year's duration.

Twenty-one years before admission the patient had an attack of red, swollen joints that lasted five or six weeks and was followed by three months of semi-invalidism. He was well except for occasional stiffness of the joints until eleven years before admission, when he had another similar attack of rheumatism. Several teeth were removed following the attack, and he had had no joint troubles since then. One year before admission he first noted that he became short of breath easily and sweated profusely on the slightest exertion. This condition slowly increased in severity. Two months before entry he had several attacks of acute shortness of breath and consulted a physician, who prescribed digitalis (1 pill three times a day). About then he noticed swelling of the feet and ankles each morning. He continued to work until two weeks before admission, when he consulted another physician, who put him to bed.

Except for the attacks of rheumatism, his past history was negative. One sister died of heart trouble at the age of fifty-eight. His wife had had four pregnancies: the second ended in a miscarriage, in the third, premature twins died shortly after birth, and the other two children were living and well.

Physical examination showed a well-developed and well-nourished man with slight orthopnea but without cyanosis or dyspnea. There was slight engorgement of the neck veins. There were numerous moist rales and dullness at each base. The heart was greatly enlarged to the left, with a diffuse apical impulse at the fifth interspace, 14 cm. from the midsternal line. The right border was 3 cm. from the midsternal line. The rate was regular, and the sounds of poor quality, with a short, high-pitched systolic murmur at the apex. No diastolic murmur or thrill was heard. The

liver was felt 3 to 4 cm. below the costal margin. The spleen was not felt. There was slight pitting edema of the ankles.

The blood pressure was 160 systolic, 110 diastolic. The temperature was 98.6°F., the pulse 80, and the respirations 21.

Examination of the blood revealed a red-cell count of 5,000,000, with a hemoglobin of 75 per cent, and a white-cell count of 11,300, with 61 per cent neutrophils. The urine was negative. A blood Hinton test was negative. An electrocardiogram showed normal rhythm, at a rate of 90, with left bundle-branch block and prominent T waves. A chest roentgenogram showed that the heart lay horizontally in the chest and was greatly enlarged, the enlargement chiefly involving the left ventricle. The pulmonary conus was prominent. The outline of the heart was indistinct because of a rather hazy type of dullness that involved the greater portion of the lungs and was most marked at the right base. The diaphragm was indistinct but appeared to be in the usual position and to move fairly well with respiration. The transverse diameter of the chest was 27.6 cm., and that of the heart 18.9 cm.—6.1 to the right and 12.8 to the left.

The patient improved a great deal on rest, digitalis and ten daily injections of 50 per cent glucose, and was discharged after a period of two weeks. The haziness in both lung fields had definitely cleared.

Second admission (two and a half years later). The patient improved for a short time after discharge but then began to have spells of nocturnal dyspnea and slight orthopnea. The dyspnea increased and the edema became progressively worse so that he was confined to bed for a twenty-month period. His legs were tapped many times by his physician, who at one time removed 18 liters during a period of twenty-four hours. The chest was tapped three times. Salyrgan and other diuretics were given effectively. About one year before this admission the patient had improved somewhat and was able to sit around the house. He had had an abdominal tap about every two weeks during the previous year and had taken 3 gr. of digitalis a day (recently, 7½ gr. a day).

Physical examination showed that the heart was still greatly enlarged. The rate was variable; at times it was 60 and then quite suddenly jumped to somewhat over 80, with some extrasystoles. The sounds were poor, and no murmurs were heard. There were rales at the lung bases, and signs of fluid at the left base and in the abdomen. The liver was felt 11 cm. below the right costal mar-

*On leave of absence.

gin. There was tremendous porky edema of the legs, and considerable congestion of the neck veins.

The blood pressure was 130 systolic, 65 diastolic.

The red-cell count was 5,480,000, with 80 per cent hemoglobin, and the white-cell count 11,800, with 86 per cent neutrophils. The serum protein was 7.3 gm. per 100 cc. An abdominal paracentesis yielded 6000 cc. of clear, straw-colored fluid. A left chest tap at the angle of the scapula in the seventh interspace yielded bloody fluid, which continued to be bloody and later became xanthochromic.

A chest roentgenogram showed marked enlargement of the heart involving all chambers, most marked in the region of the left ventricle. The right border had a double contour, probably owing to prominence to the right of the left auricle. The posterior mediastinum was also obliterated by auricular enlargement. The pulsations of the heart were extremely weak and diffuse fluoroscopically. When the patient was placed in a prone position the mediastinal shadow changed, becoming broader across the base. The aorta was of normal size. There was considerable air in the left pleural cavity. The left lung seemed about one quarter collapsed. There was also fluid in the left pleural cavity, the level being at the eighth rib in the anterior axillary line. The hilar shadows on both sides were grossly increased in width and density. There was a calcified lymph node in the right axilla. The electrocardiogram continued to show left bundle-branch block.

On the eleventh day a friction rub was heard at the apex area that was confined to diastole and did not disappear on full inspiration. The following day the rub was to-and-fro, being distinct in diastole and systole.

The patient responded to digitalis and diuretics and was discharged on the fifteenth hospital day.

Third admission (four and a half years later). After leaving the hospital the patient remained in bed for about six months but then was able to get up and around; he became very dyspneic on exertion although no more so than formerly. He always had to sleep on several pillows at night. During this interval he frequently accumulated fluid, which was controlled fairly well by diuretics of one sort or another. Three weeks before re-entry he began having a cough productive of white frothy sputum; his legs began to swell, and the dyspnea became so severe that he re-entered the hospital.

Physical examination showed a pale, orthopneic man with labored respirations. There were di-

minished voice sounds, breath sounds and dullness over the left chest anteriorly and posteriorly. The apex impulse of the heart was not seen or felt. The left border of dullness was not made out. The aortic second sound was equal to the pulmonic. The heart sounds were of poor quality, with a rate of 40 at both apex and wrist; the rhythm was normal. There was heavy pitting edema with elephantiasis of both legs.

The blood pressure was 140 systolic, 80 diastolic. The pulse was 40, and the respirations 28.

The red-cell count was 4,800,000, with 90 per cent hemoglobin. The total protein was 6.79 gm. per 100 cc., with an albumin-globulin ratio of 1.54. An electrocardiogram showed a 2:1 block, with left bundle-branch block and left-axis deviation.

A chest roentgenogram showed marked change in the appearance of the heart. It had definitely increased in size, particularly in the region of the superior portion of the right ventricle, with the formation of a localized bulge in this area. There was fluid in the left chest, and slight displacement to the right.

The patient again responded well to digitalis and diuretics and was discharged in three weeks.

Fourth admission (fourteen months later). The patient returned for symptomatic relief of congestive failure.

Physical examination showed a pale man with rather marked respiratory difficulty sitting up in bed. There were moist rales, increased dullness and absent breath sounds over the left chest, both anteriorly and posteriorly, and medium moist rales over the right base. There were no further changes in the examination of the heart. The liver was felt four fingerbreadths below the costal margin. There was elephantiasis of both legs.

The blood pressure was 105 systolic, 55 diastolic.

The red-cell count was 5,030,000, with 92 per cent hemoglobin, and the white-cell count 9200.

A chest roentgenogram showed fluid in the left pleural cavity displacing the heart to the left. The left border of the heart was incompletely visualized. An electrocardiogram showed auricular fibrillation, with complete block and right bundle-branch block.

The patient remained in the hospital for three weeks, on restricted fluids and diuretics, and lost 37 pounds of fluid.

Fifth admission (six months later). At home he continued to take digitalis but diuretics were administered with difficulty because of his poor veins. He had received not more than three intravenous administrations of Salyrgan in the interval and had been reduced to the rectal and intramuscular

use of this drug. He gradually accumulated a large amount of fluid and became much more dyspneic, even at rest.

Physical examination had not changed appreciably. There were marked ascites and peripheral edema. The heart rate was 40 and there were signs of pleural effusion on the left. An electrocardiogram showed auricular fibrillation with complete auriculoventricular block and left bundle-branch block, the ventricular rate equaling 40.

A chest roentgenogram showed that the heart had not appreciably changed. There was slightly more fluid in the left chest than previously and the pulmonary vessels appeared more engorged. There was the marked thickening of the pleura on the left that had been present on all the previous films. Fluoroscopy showed that the right ventricle was still unusually large in its upper portion.

On a regime of bed rest, digitalis, ammonium chloride and Salyrgan, the patient improved rapidly and lost 40 pounds of fluid. He was discharged in three weeks.

Final admission (two and a half years later, at the age of fifty-four). The patient was followed at home by his physician, receiving digitalis, ammonium chloride and Mercupurin, and did well under this regime until two months before admission, when he gradually began to retain fluids and developed increasing edema of the legs and breathlessness. Five days before entry he developed cough productive of pink, frothy sputum, and on the night before admission he became so orthopneic that he was unable to sleep and thought he was going to smother to death.

Physical examination showed a pale, extremely dyspneic man in marked congestive failure. The neck veins were markedly distended in the upright position. The chest was barrel shaped, with flatness to percussion and absent breath sounds in the lower left chest. On the right there were coarse, bubbling rales at the base. The heart was enlarged to the anterior axillary line, the sounds were distant, the rhythm was very irregular, but no murmurs were heard. The abdomen was distended and tympanitic. The liver was not enlarged to percussion and the spleen was not palpable. The peripheral edema extended to the groin.

The blood pressure was 105 systolic, 56 diastolic. The apex rate was 76.

The red-cell count was 5,150,000, with a hemoglobin of 16 gm., and the white-cell count 33,400, with 92 per cent neutrophils.

The patient failed to respond to the usual measures and died approximately twenty-four hours after admission.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM W. BECKMAN: In spite of the fact that many features of this case confused me when I went over it, I am relatively certain, because of the symptoms of dyspnea and edema, the physical signs of enlarged heart confirmed by x-ray and the electrocardiographic evidence of increasing conduction difficulty, that the patient was suffering from heart disease and, of course, that he had congestive failure. Dr. Paul D. White always teaches that one is supposed to make not only a functional diagnosis, which would be congestive failure, but also a diagnosis of the structural abnormality of the heart and of the etiology or the condition producing the structural and functional abnormalities.

So far as etiology is concerned, there are a number of things one need not consider because of the extreme duration of the congestive failure. The patient had some degree of congestive failure for thirteen years without any remissions. It is only necessary to mention congenital heart disease in passing. He might possibly have had an interventricular septal defect that ultimately led to left ventricular hypertrophy and failure; but it is unusual for congenital heart disease to wait for forty-two years to manifest itself. Also, the complete absence of cyanosis anywhere in the story is very much against a septal defect, because if the left ventricle fails the pressure in it falls below that on the right and unoxygenated blood is forced into the peripheral circulation to produce cyanosis. The same argument holds for cor pulmonale. The absence of cyanosis, polycythemia and evidence of right ventricular preponderance makes it unnecessary to give this diagnosis more than passing consideration. Again, the duration is too long for syphilis. Also there is no characteristic murmur of aortic regurgitation, and the serologic tests for syphilis were negative.

At the time of the first admission the patient had a blood pressure of 160 systolic, 110 diastolic, which represents true hypertension, and, as often happens, the first thing that drew attention to the high blood pressure was the presence of congestive failure. However, I do not believe that hypertension alone could account for this degree of failure extending over thirteen years, but it doubtless was a contributing factor.

Arteriosclerosis and coronary heart disease must also be considered. The presence of bundle-branch

block favors this diagnosis. The absence of characteristic T-wave changes in the electrocardiogram, and particularly the complete absence of mention of anginal pain anywhere in this long abstract, make the diagnosis of coronary heart disease untenable as the explanation for twelve years of congestive failure. I think the presence of pain in the joints is of significance in the etiology of the type of heart disease. In the first place, the way the attacks of joint pain are described is characteristic of rheumatic fever; it is much more like that than like rheumatoid arthritis. He had two distinct attacks of rheumatic fever and probably some activity between the attacks, as evidenced by the intermittent joint pains. Since it is well known that few people have two attacks of rheumatic fever without some heart disease, it is probable that he at least had myocarditis. Another thing in favor of rheumatic heart disease is the duration, for on the law of averages people who stay in congestive failure for prolonged periods of time have rheumatic heart disease oftener than any other type of heart disease. That, of course, is just on the basis of statistics and may mean nothing in this particular case.

Another thing in favor of rheumatic heart disease is the conduction difficulty, which ended in auricular fibrillation. Auricular fibrillation is one of the common features of rheumatic heart disease, particularly in cases in which there is mitral stenosis. Another thing that might be explained on the basis of rheumatic heart disease is the development of pericarditis. The patient may have had pericardial effusion at the time of the second admission, judging from the x-ray film. Later on during the admission he developed a definite friction rub, which seemed to be pericardial and not pleuro-pericardial. All this is in favor of rheumatic heart disease. Regardless of whether that was the fundamental thing, he doubtless had some residual myocardial fibrosis as the result of the previous attacks of rheumatic fever.

Strongly against the presence of rheumatic heart disease, however, is the complete absence of murmurs throughout the twelve years that the patient was followed, except for one occasion, at the time of his first admission, when they mentioned an apical systolic murmur to which no one attached significance. However, for no heart murmurs to have been heard is not incompatible with rheumatic heart disease, because all the reported examinations in this record were done when the man was in severe congestive failure. Frequently, in failure, one does not hear a murmur even though there is valvular disease. In favor of rheu-

matic heart disease is the x-ray evidence of an extremely large left auricle. The roentgenologists say that that is very good evidence for mitral stenosis. However, he did not show anything except two elevated white-cell counts to suggest true rheumatic activity during the twelve years. There was no prolongation of the PR interval, no joint pain or anything else that suggests rheumatic activity.

Against the whole thing's being on the basis of congestive failure is the fact that pleural effusion was always on the left side. We are taught that, if unilateral effusion is present as a part of heart failure, it is on the right side rather than the left. It was always on the left in this case. The fact that the fluid was bloody and xanthochromic is highly unusual for fluid in congestive failure, and suggests that some other process was present. However, it is known that the patient had had three chest taps shortly before that admission, and at the time of admission there was air in the chest, which may have indicated that previous taps had damaged the lung and had allowed blood to escape into the pleural space. We therefore cannot put too much weight on the bloody fluid.

I cannot fit two factors very well into the diagnosis of rheumatic fever. One is the fact that the patient showed a thickened pleura in all the films. Another thing is the bulge that developed on the right ventricle, as seen by x-ray. I think that this is a good time to have the x-ray films exhibited, because I need a lot of help from them.

DR. MILFORD SCHULZ: These are the films taken at the first and second admissions. They are all anteroposterior views. There are also a good many oblique views that we might have use for later.

DR. BECKMAN: Can you be sure that the left auricle was enlarged, or must you rely on the fluoroscopist?

DR. SCHULZ: In the right antero-oblique view there seems to be definite enlargement posteriorly in the region of the left auricle.

DR. BECKMAN: You are quite sure that it is the left auricle?

DR. SCHULZ: It is in the position that the auricle usually occupies. I think that the patient was undoubtedly fluoroscoped and that the person who interpreted the examination took the fluoroscopist's opinion into consideration.

DR. BECKMAN: Where is the bulge on the right ventricle?

DR. SCHULZ: This is the right antero-oblique film, and I believe that this represents the bulge in the area of the right ventricle anteriorly.

DR. BECKMAN: Do you suppose it could be an aneurysm?

DR. SCHULZ: It was not present previously. How frequently does an aneurysm occur in the right ventricle?

DR. BECKMAN: Almost never, but I have to explain it some way.

How about the prominence of the left auricle in the earlier films? Is it really the left auricle, or has it some connection with the later shadow in the ventricle?

DR. SCHULZ: I should say that it was the left auricle. This homogeneous increase in density may be fluid in the left chest. You can see it extending along the lateral chest wall. Or perhaps it is thickened pleura.

DR. BECKMAN: That was said to be present in all films, although they mentioned it only at the end.

DR. SCHULZ: It had been present since the time of the pneumothorax.

DR. BECKMAN: I do not know whether it is possible to say that the thickened pleura was due simply to the fact that the lung was traumatized and blood went into the thorax to cause sufficient irritation to give thickening. It may have been due to some other process, although I am at a loss to explain it.

I shall have to guess concerning the bulge in the right ventricle. As I have said, an aneurysm in this region is very uncommon. Aneurysms are usually the result of coronary heart disease with a cardiac infarct. At the admission prior to the one when the bulge in the right ventricle was noted, a friction rub was heard. This might possibly have been the result of infarct, perhaps even in the right ventricle, which thereafter led to weakening and subsequent development of an aneurysm. However, I do not believe that it is possible to make a diagnosis of coronary disease in the complete absence of precordial pain throughout the history, particularly at the time the rub appeared. There would have to be more evidence of coronary disease than he had to lead to the diagnosis of coronary occlusion.

The only other thing I can think of is a tumor in the right side of the heart. There are a wide variety of primary tumors, and every kind of metastatic tumor has been seen in the heart. I do not know how one can differentiate primary tumors of the heart, but I shall "stick out my neck" and say that this patient had a benign tumor in the right ventricle. I presume that he had mitral stenosis on the basis of the previous attack of rheumatic fever and the x-ray evidence of mitral

stenosis, although a murmur was never heard. I believe that the lungs will show pulmonary edema. The white-cell count of 32,000 terminally means that he had some acute infection, probably bronchopneumonia. He might have had acute bacterial endocarditis, but there is no evidence for that, and I think pneumonia is far commoner in occurrence. I also think that there was cardiac cirrhosis of the liver on the basis of the fact that the liver was so large at the onset and was not palpable at the final admission.

DR. BENJAMIN CASTLEMAN: Dr. Williams, would you like to comment?

DR. CONGER WILLIAMS: I know the answer. There is just one thing that I should like to say. I remember seeing this patient on the ward when I was a house officer several years ago. At that time the diagnosis of coronary heart disease was questioned because of the duration of symptoms. It was also pointed out that the electrocardiogram, which then showed bundle-branch block, could very well conceal any underlying difference in preponderance of the ventricles. As soon as bundle-branch block appears, axis deviation is no longer significant. The new pattern bears no relation to ventricular preponderance and may conceal a high degree of right or left preponderance.

CLINICAL DIAGNOSES

Arteriosclerotic heart disease, with right and left congestive heart failure.
Pleural effusion, left.

DR. BECKMAN'S DIAGNOSES

Rheumatic heart disease, with mitral stenosis.
Congestive heart failure.
Thickened pleura, possibly due to hemothorax.
Bronchopneumonia.
Cardiac cirrhosis.
Benign tumor of right ventricle?

ANATOMICAL DIAGNOSES

Pulmonary arteriosclerosis, severe, arterial and arteriolar.
Ayerza's disease.
Pulmonary embolism, old, left (? thrombosis).
Mural thrombus of right atrium.
Cor pulmonale.
Organizing blood clot, left pleural cavity.
Mural endocarditis, fibrous.
Pericarditis, fibrous.
Bronchopneumonia.
Peripheral edema.
Passive congestion of liver, spleen and kidneys.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: This man had an enormous heart, weighing 750 gm. The enlargement for the most part was on the right side. The right auricle was tremendously enlarged, and there was

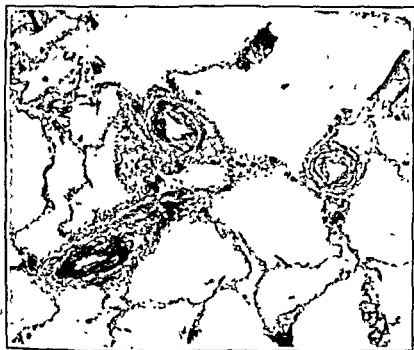


FIGURE 1. Photomicrograph of Lung Showing Arteriosclerosis.

a mural thrombus in the appendage. The right ventricle was tremendously dilated and thickened, measuring 7 mm. in thickness, which is at least twice normal. The left auricle was not enlarged; neither was the left ventricle. We were unable to find any abnormalities in the valves. The ring of the tricuspid valve was greatly dilated, measuring 16 cm. in circumference. The pulmonary valve was also somewhat dilated, and the conus below it was markedly dilated, forming an aneurysmal outpocketing approximately 1 cm. deep. The endocardium over it was thickened and fibrous, but the underlying myocardium was normal. The appearance of the endocardium was similar to that seen below the aortic valve in the left ventricle in cases of long-standing aortic regurgitation. The coronary arteries showed only slight sclerosis. Grossly we were fairly certain that the etiology of the enlargement of the heart was in the lungs and not in the heart.

On examination of the pleural cavities we were amazed to find a large mass, about 9 by 8 by 8 cm., in the lower part of the left pleural cavity extending from the diaphragm up to the fourth rib. It was adherent to the pleura and pushed the left lower lobe medially and anteriorly; it also pushed the heart over a bit. This proved to be an organizing hematoma, which apparently must have occurred at the time of one of the chest taps

before the second admission, as Dr. Beckman suggested. There was no fluid in the left pleural cavity. The lungs in gross showed a moderate degree of arteriosclerosis of the main vessels, but microscopically there was severe arteriolarsclerosis. This slide (Fig. 1) is a low-power view of a section of the lung showing three arteries with markedly thickened walls and intimal hyalinization. The intervening lung is normal. The next slide (Fig. 2) is a high-power view showing the luminal narrowing. The findings are those of the Ayerza syndrome and explain the right-sided cardiac hypertrophy. There was, in addition, a terminal

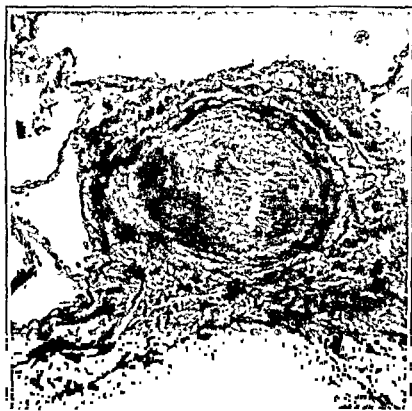


FIGURE 2. Photomicrograph of High Magnification Showing a Vessel with Marked Luminal Narrowing.

bronchopneumonia and a large, laminated, old, adherent embolus in the left main pulmonary artery and its two major branches, apparently arising from the mural thrombus in the right auricle. It may have originated in situ as a thrombus, but I believe that most cases of thrombosis of the large pulmonary arteries begin as emboli and build up by superimposed thrombosis. It was an old affair and had nothing to do with the terminal event; but it certainly added to the burden of the right heart. The liver showed moderate congestion but no cirrhosis.

I think the suggestion by Dr. Williams that the bundle-branch block disturbed the axis deviation certainly held here. If he not had it, there certainly would have been a marked right-axis deviation.

CASE 29352

PRESENTATION OF CASE

A seventy-seven-year-old baker entered the hospital because of severe dyspnea.

Approximately twenty or thirty years prior to admission the patient began to suffer with mild dyspnea on exertion that became progressively worse. About four and a half years before entry he was seen in the Out Patient Department, where a few wheezes and rales were heard in his chest. The heart sounds were distant. The aortic second sound was greater than the pulmonic; there were no murmurs. The blood pressure was 140 systolic, 85 diastolic. He complained of moderate urinary frequency. The diagnoses of pulmonary emphysema, arteriosclerotic heart disease and early decompensation were made. He was digitalized, with improvement of his symptoms. After that he was quite well, except for a chronic cough productive of small amounts of gray sputum daily, until one month prior to admission, when he developed epigastric pain, gas and constipation. Because of the constipation his physician stopped digitalis and referred him for gastrointestinal studies. He rapidly became dyspneic and orthopneic. He had no nocturnal attacks or chest pain. The chronic cough became worse, and the patient raised one cupful of gray sputum daily. There was no nausea, vomiting, anorexia or tarry, bloody or clay-colored stools. There was no fever, hemoptysis, weight loss or chills.

The family and past histories were noncontributory.

Physical examination revealed a well-preserved old man who sat up in bed because of moderate dyspnea. He coughed frequently and brought up small amounts of foul-smelling, yellow sputum. The chest was hyperresonant. The heart was percussed 10.5 cm. to the left of the midsternal line in the fifth intercostal space. The sounds were distant and there were many extrasystoles. There was a soft, blowing systolic murmur over the entire precordium and in the left axilla but best heard at the apex. The neck veins were slightly distended. There was slight dullness at the base of the left chest posteriorly, and in that area the voice and breath sounds were slightly suppressed. The abdomen was soft; no masses were felt, and no tenderness elicited. There was pitting edema at the ankles.

The blood pressure was 120 systolic, 70 diastolic. The temperature was 99°F., the pulse 90, and the respirations 25.

Examination of the blood revealed a red-cell count of 4,500,000, with a hemoglobin of 14.5 gm.,

and a white-cell count of 7500, with 75 per cent neutrophils. The urine and stools were negative. A blood Hinton test was negative. The serum protein was 6.3 gm., and the nonprotein nitrogen 70 mg. per 100 cc.; the carbon dioxide combining power was 21.0 millimols, and the chloride 975 milliequiv. per liter.

A gastrointestinal series was negative. Chest roentgenograms showed haziness over almost all of both lung fields consisting of strand-like infiltration following the pathway of the broncho-vascular tree. In addition, in the right lower lobe there was an area of increased density 5 cm. wide and 3 cm. high, with indefinite margins. There was calcification of some of the hilar lymph nodes on the right. There was a small amount of fluid in the left pleural cavity, and probably some in the right. The heart was enlarged, especially in the region of the left ventricle, and the aorta was tortuous.

An electrocardiogram showed a normal sinus rhythm of 75. The PR interval was 0.16 second. The ST segment was depressed in Leads 1, 2 and 4. The T wave was low in Leads 1, 3 and 4, and there was slight left-axis deviation.

The patient was digitalized and given mercurial diuretics, following which the edema lessened. On the ninth hospital day oliguria developed and the nonprotein nitrogen was found to be 116 mg. per 100 cc. The nonprotein nitrogen gradually rose, and complete urinary suppression developed on the eleventh hospital day. Catheterization yielded only 2 cc. of urine. He was given Mercupurin and 50 cc. of 50 per cent glucose solution. On the thirteenth hospital day the nonprotein nitrogen was 160 mg. per 100 cc., the carbon dioxide combining power 19.7 millimols per liter and the chloride 93.2 milliequiv. per liter. The patient showed increasing signs of uremia, remained anuric for four days and died on the fifteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. JACOB LERMAN: I should like to know what the urine showed, even though it was said to be negative.

DR. BENJAMIN CASTLEMAN: At the first examination it was amber and alkaline, with a specific gravity of 1.025, and showed no albumin or sugar. The Sulkowitch test for urinary calcium was ++. On the following day the specific gravity was 1.010, and on the fifth day 1.007; there were no other changes.

DR. LERMAN: The diagnoses made in the Out Patient Department—arteriosclerotic heart disease, cardiac failure and pulmonary emphysema—seem justified on the basis of the findings at

that time. The patient's condition remained unchanged until he developed evidence of pulmonary infection. At that point we may say that, as so commonly happens in people with long-standing congestive failure, chronic bronchitis developed. Later he developed epigastric pain, which suggested to the doctor the need for gastrointestinal studies.

The physical findings indicate a dilated heart with congestive failure and fluid in the left chest. The electrocardiogram suggests obvious digitalis effect and slight coronary disease. The blood findings are normal. To me the striking laboratory findings are the retention of nitrogen and the mild acidosis in the presence of an apparently normal urine. The specific gravity was 1.025, indicating fairly good concentration, at least in the beginning. X-ray study confirmed congestive failure and showed something else, which may have been a pulmonary tumor.

DR. MILFORD SCHULZ: These films show a somewhat enlarged heart with particular prominence in the left ventricular area. There is some fluid at both bases, and the hilar and pulmonary markings are increased. In addition, this area of infiltration apparently lies in the midportion of the right lower lobe.

DR. LERMAN: Is the area in the right lower lobe consistent with bronchiectasis, or is it not extensive enough?

DR. SCHULZ: Some of the markings at the bases are consistent with bronchiectasis. I think the area of infiltration is something more recent—perhaps an infarct.

DR. LERMAN: The x-ray findings are consistent with congestive failure plus the additional shadow in the right lower lobe, which Dr. Schulz suggests may be a pulmonary infarct. It may be a tumor. Certainly the clinical findings are consistent with bronchiectasis at both bases in a man with long-standing congestive failure.

The point I must explain is why this patient had renal failure in the presence of a normal urinary picture. It seems difficult. I cannot see any connection between the shadow in the right lower lobe and the renal involvement. The x-ray findings of an apparently prominent left ventricle and the accentuated aortic second sound noted in the record suggest the existence of hypertensive heart disease. We have no evidence from the record that he had hypertension, and it does not seem likely that a slight degree of congestive failure existing four and a half years before entry could have dropped the blood pressure from a hypertensive to a normal level. Therefore, I doubt that he had hypertensive heart disease. Arteriosclerotic heart disease is the more likely explanation of the cardiac picture.

I should like to consider chronic glomerulonephritis as an explanation of renal failure. It is most unlikely that he would not have albuminuria or show slight evidence of nephritis in the sediment. Furthermore, the concentration of the urine to 1.025 is hardly consistent with chronic glomerulonephritis. There is no obvious evidence of arteriolar nephrosclerosis or of pyelonephritis. The absence of hypertension certainly argues against glomerulonephritis, nephrosclerosis and pyelonephritis.

The final episode of oliguria and anuria could have been due to the natural course of uremia, but we must remember that he was taking mercurial diuretics and that these may have caused additional irritation of the kidneys and contributed to their final shutdown. I am inclined to believe that at autopsy there was evidence of irritation of the kidneys due to the diuretics. This, however, does not help to explain the discrepancy between renal failure and normal urinary findings. Cardiac failure alone does not explain it. Cardiac failure plus pulmonary infection in the presence of arteriosclerotic kidneys might explain the picture.

Other mechanisms, extrarenal in origin, may produce renal failure without actual injury of the kidneys. Dehydration is one of them, but it obviously does not play any role here. Adrenal failure sometimes causes marked nitrogen retention without renal damage. I have never seen this degree of renal failure—a nonprotein nitrogen of 70 mg. per 100 cc. and a carbon dioxide combining power of 21 millimols per liter—in adrenal disease. Moreover, the blood chloride was within normal range, and there was no hypotension.

One should consider some process involving both ureters simultaneously. Infection may do it, but there is no evidence of it here. I cannot conjure up anything else,—malignant disease or any other pathologic process,—that would involve both ureters uniformly. One would have to assume that the patient had congenital absence of one kidney or of one ureter with involvement of the remaining kidney or ureter by a malignant process, such as retroperitoneal lymphoma. This seems somewhat farfetched.

One must also consider bilateral ischemia of the kidneys. Among the possible causes of this condition is some disturbance of the aorta itself. Aneurysms, in the proper location, have been described that produce progressive ischemia of the kidney with renal failure and eventual shutdown. This patient had pain in the epigastrium. He may have had a dissecting aneurysm of the thoracic aorta that worked its way down to both renal arteries and then caused progressive shutdown. Against this diagnosis is the fact that the pain

was not excruciating and did not persist. Furthermore, there was no evidence of arterial involvement elsewhere: there is no mention of obstruction of the iliac arteries.

One might consider a horseshoe kidney as a cause of progressive renal failure without much in the way of urinary findings. However, since there is no mention of an abdominal mass we need not consider it further.

It seems to me that the most likely diagnosis is arteriosclerotic heart disease with congestive failure, and arteriosclerotic kidneys with renal failure resulting from congestion plus the toxic effect of chronic pulmonary infection. I meekly add the possibility of an aortic aneurysm producing bilateral renal ischemia.

CLINICAL DIAGNOSIS

Arteriosclerotic heart disease, with decompensation.

DR. LERMAN'S DIAGNOSES

Arteriosclerotic heart disease, with congestive failure.

Uremia due to congestion of arteriosclerotic kidneys plus toxic effect of chronic pulmonary infection.

Bilateral renal ischemia due to aneurysm of aorta?

ANATOMICAL DIAGNOSES

Undifferentiated malignant tumor involving retroperitoneal lymph nodes, lungs, pleura, spleen, peritoneum and vertebral bone marrow.

Compression of both ureters by tumor.

Hydroureter, right.

Hydronephrosis, right.

Cardiac hypertrophy, moderate.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy this man showed perfectly normal-looking kidneys, except for slight scarring such as one might expect to find in a man of his age. The right pelvis was dilated, but the left was not. The retroperitoneal nodes all along the aorta were enlarged, were replaced by tumor and compressed both ureters, the right more than the left. We were unable to get a probe into the right ureter at a point about 6 cm. below the ureteropelvic junction. A similar process was present on the left, but the occlusion was not so complete because it was easily probed. However, with the probe out, the walls of the ureter closed down on the lumen, so that during life there was probably complete obstruction. It is possible that the complete occlusion on the right side produced so-called "reflex anuria" on the other side so that no urine reached the bladder, but the urologists inform me that this rarely, if ever, occurs.

The shadow in the right lower lobe was a markedly thickened pleura infiltrated with neoplasm. There were nodules of tumor in the lung parenchyma, in the spleen, in the omentum and in the mesentery; and microscopically they were present in the vertebral bone marrow. The strand-like infiltration observed on the roentgenogram was due to tumor infiltration of the lymphatics.

The exact classification of the tumor is difficult. The cells are large, many with two or three nuclei, and although it suggests in a few places an embryonal form of carcinoma, such as is seen in the testis, it is probably some form of undifferentiated sarcoma. The testes were normal, and we were unable to find any other primary source, so that we shall have to leave it as an undifferentiated malignant tumor.

The heart was moderately enlarged and showed minimal coronary disease. There was no evidence of disease within the kidney itself.

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INFECTIOUS DISEASE IN WARTIME

THE current educational campaign of the Metropolitan Life Insurance Company has for its subject, suitably enough under present conditions, rheumatic fever. To achieve the objectives of an earlier recognition of rheumatic fever, better care of the child ill with the disease, and an appreciation of the increased dangers resulting from overcrowding and the unsanitary conditions following in the wake of our organization for war, the company has planned a most comprehensive program. This includes the distributing of suitable material to policyholders and others, the enlisting of the interest of local physicians and school officials and

the arranging of discussions at parent teacher associations, service clubs and so forth. In addition, an excellent pamphlet on the clinical considerations of rheumatic fever has been prepared for distribution to physicians. In this country the best approach to any public problem is still the education of the public.

Rheumatic fever remains a major health problem today. Between the ages of five and nine years it causes more deaths than any other single disease, and is exceeded in mortality only by a combination of the four principal communicable diseases of childhood. Between the ages of ten and fourteen years it is also outranked by none, and between fifteen and twenty-four years it is led only by tuberculosis. It is fair to say, however, since the inference may be drawn that rheumatic fever is actually on the increase, that its relative growth in importance is due to the fact that deaths from other diseases have declined even more rapidly. Actually the death rate from chronic heart disease among the company's policyholders between the ages of five and twenty-four has fallen two thirds in the last thirty years, and that due to acute rheumatic fever at approximately the same rate—from 72 to 17 per 100,000.

The disease rheumatic fever has richly earned the significance that is being attached to it and the efforts that are being made to defeat it. There is, however, reason to doubt that at the present time any important infectious disease is undergoing a drop in its morbidity rate. In the armed forces, composed largely of men under thirty and including such a large proportion of the group in the later years of adolescence, rheumatic fever constitutes a constant and relatively serious medical problem. Everyone is aware of the increase in communicable diseases, particularly of scarlet fever,—fortunately in a mild form,—of meningitis and of pulmonary infections.

The same general experience obtained during World War I, and it is, of course, common knowledge that war with its mass movements of population, its mobilization in close quarters of large

numbers of susceptible individuals and its tendency to break down the usually well-organized civilian health facilities, carries with it an inevitable increase in the microscopic enemies of man, regardless of the justice of the cause to which the Nation is committed.

For some time to come the acute infectious diseases must be combated—as they have been for years; and it is hoped that more effective weapons will be available than have ever before been possessed. There is every indication, also, that outbreaks of malaria and other tropical and semi-tropical diseases must be faced when the troops return from their far-flung battle lines.

A NURSE ON BATAAN AND CORREGIDOR

LIEUTENANT REDMOND,* formerly an American Red Cross nurse, now an officer in the Army Nurse Corps, went to Manila in September, 1940, after three years of service in the Army and Navy Hospital at Hot Springs, Arkansas. Little did she realize what her experiences would be when, after a year, she found herself in the Sternberg General Hospital in the fall of 1941. Her wards were going like clockwork at seven o'clock in the morning of December 8 when she came off duty, and she had planned a morning of sleep and an afternoon of golf. The attack on Pearl Harbor, when reported over the telephone by a friend, was at first taken as a joke, but by some sensible instinct she rushed to the bank and cabled her savings home. No sleep came that day and for many days to come. Soon hundreds of casualties arrived in trucks, ambulances, buses, carts and anything that had wheels. Many were dead when they reached the hospital. Operating tables were empty hardly a moment at a time. The morale was magnificent. The wounded were quiet. Often one would say, "Take my buddy, he's hurt worse than me."

The bombing continued. Nurse Redmond

watched some dogfights in the sky and saw three enemy planes brought down. The pilots, dead, were brought to the hospital; one was a German. Cavite was burning. Soon rumors spread, only to be followed by Japanese troops marching on Manila. By December 23, Nurse Redmond and her associates had been moved to Bataan. There she remained, conscious of the slowly approaching danger but always doing her full duty. Supplies grew short, the field hospitals were bombed, the dust and heat were indescribable. With a hospital full of dysentery patients, they had no lime for the latrines. Serum for gas gangrene ran out, and Colonel Adamo's patients had to be transferred to a hill away from the hospital sheds. Finally came the air raids, blowing some of the wards to bits. Foxholes were dug outside each building and used by all who could get to them; others crawled under the beds in the orthopedic ward after the traction ropes had been cut. Then came the care of the twice wounded. Fortunately Nurse Redmond was uninjured, although knocked down and buried in debris. Little work could be done for a day or two, except to bury the dead.

Like most persons in a crisis, one begins to think "long thoughts," and Nurse Redmond was no exception.

That night we stayed in our fox holes. I didn't sleep. We hadn't eaten since breakfast, but I wasn't hungry. We were like hunted animals, waiting for the kill, almost hoping it would happen quickly so that the torment of waiting would end. But stronger than that was anger; anger and hate and a hot desire to fight back, to avenge our dead.

What kind of human beings would deliberately bomb a hospital, defenseless, openly marked for what it was, filled with the wounded and the sick?

I don't know. The only answer I had found when I crawled out of my hole in the morning, my head aching, a crick in my back, my legs cramped, was not an answer but a conviction. This isn't a war in which anybody—anybody—is let off. Each single individual of us is in it and each must give everything he has to give. An enemy that will bomb hospitals and undefended cities—sick and injured men, or women and children and helpless old people—isn't an enemy you can ever come to terms with; not in the usual meaning of the phrase. The war must end without compromise.

After more horrors, Bataan fell, and on April 7, Nurse Redmond was moved to Corregidor. There

*Redmond, J. *I Served on Bataan*. 167 pp. Philadelphia and New York J. B. Lippincott Company, 1943.

she worked in a hospital tunnel, always cheerful, always doing what she could to serve her patients. There were some amusing moments. Food was better at first than on Bataan. A cleaning woman found some soap and nail polish, so the nurses had shampoos, finger waves and manicures. Some dresses were discovered, and they had a rummage sale. A Chinese tailor who had taken refuge in the tunnel proved to be a great find. He fashioned suits out of discarded officers' clothes, so the nurses had streamlined coveralls, skirts and blouses. Finally came the shelling of Corregidor, and even Nurse Redmond found it hard to face great numbers of people torn and bleeding and dying in masses. "When one patient dies it is agonizing enough, when you are faced by such mass suffering and death something cracks inside you, you can't even be quite the same again."

At last came the trip by air to Melbourne, Australia, leaving Corregidor on a strangely quiet night when the Japanese were celebrating the Emperor's birthday. General Wainwright's car led the small procession to the docks. The flight to Australia was as smooth and peaceful as if there were no war.

MEDICAL EPONYM

CLUTTON'S JOINTS

This disease is described by H. H. Clutton in a paper "Symmetrical Synovitis of the Knee in Hereditary Syphilis" appearing in the *Lancet* (1: 391-393, 1886), from which the following is quoted:

To recapitulate one would say that the synovitis was symmetrical, affecting only the knees, that it was of a chronic and painless character, and that all the patients were the subjects of hereditary syphilis. It is probable that, with further observation, the knees will not be found to occupy this solitary distinction, and that other joints will be seen to be affected in a similar manner.

R W B

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BLAKE—JOHN B. BLAKE, M.D., of Brattleboro, Vermont, died August 17. He was in his seventy-eighth year.

Dr. Blake received his degree from Harvard Medical School in 1891. He taught there for a number of years and wrote on medical subjects. He was formerly surgeon in chief of the Boston City Hospital, visiting surgeon for the Long Island Hospital and consulting surgeon for the Boston Insane Hospital. He had been retired since 1920. He was a member of the Massachusetts Medical Society, American Medical Association, Boston Society for Medical Improvement, Boston Medical Library, Boston Surgical Society, Boston Obstetrical Society and American Surgical Association.

Two daughters and four sons survive.

SEED—RAYMOND C. SEED, M.D., of Lawrence, died June 6. He was in his forty-sixth year.

Dr. Seed graduated from Dartmouth College and received his degree from Jefferson Medical College of Philadelphia in 1921. He was a member of the Massachusetts Medical Society and the American Medical Association.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

TONSILLECTOMY AND POLIOMYELITIS

The Massachusetts Department of Public Health recommends the temporary postponement of tonsillectomies until an estimate can be made of the probable prevalence of poliomyelitis during the present season. Early indications pointed to a light year, but with cases on the increase in Connecticut and Rhode Island and a few cases in Massachusetts, some increase in prevalence in this state may occur. In epidemic years, numerous cases are usually reported before the middle of August. Because only a single case was recorded in the first two weeks of August, making a total of only 17 cases for the year, a large outbreak is not expected.

There is definite evidence that the bulbar form of poliomyelitis is likely to occur following tonsillectomy. The additional threat to life from this form justifies the postponement of such operations.

CHANGE IN PREMARITAL BLOOD TEST LAW

As of June 12, 1943, a new premarital blood test law became effective in Massachusetts. The underlined portions of the following copy of the law are called to the special attention of all physicians:

Section 28A. Except as hereinafter provided a certificate shall not be issued by the clerk or registrar under Section 28 until he has received from each party to the intended marriage a medical certificate signed by a qualified physician registered and practicing in the commonwealth, a physician registered or licensed to practice in any other state of the United States or a

commissioned medical officer on active service in the armed forces of the United States who has examined such party as hereinafter provided. *Such examination shall be made only to ascertain the presence or absence of evidence of syphilis, and shall include a serological test for syphilis.* Said test shall be made by a laboratory of the state department of public health or by a laboratory meeting standards approved by said department, or, if not located within the Commonwealth, approved by the United States Public Health Service. *The examination by such physician and the laboratory test shall be made not more than thirty days before a certificate is issued under Section 28.* If such physician, in making such examination, discovers evidence of any such disease, he shall inform both parties to the intended marriage of the nature of such disease and of the possibilities of transmitting the same to his or her marital partner or to their children. . . . Blank forms of medical certificates required under this section shall be furnished to city and town clerks by the Department of Public Health. . . . In emergency cases where the death of either party to the intended marriage is imminent or where the female is near the termination of her pregnancy, upon the authoritative request of a minister, clergyman, priest, rabbi or attending physician, the clerk or registrar may issue a certificate under Section 28 without having received the medical certificate, or having endorsed on his certificate a statement of such receipt, as provided by this section. Whoever, being subject to the laws of the commonwealth fails to comply with any provision of this section shall be punished by a fine of not less than ten nor more than one hundred dollars.

If the parties to the intended marriage reside in different communities in Massachusetts, the certificates should be made out in duplicate. In all other cases one certificate for each party is adequate.

DISTRICT OFFICES

With the opening of three new offices, all the eight districts of the Massachusetts Department of Public Health now have facilities where personnel assigned to the districts can meet for conferences and have a common repository for their records. Each district health officer now has a staff composed of nurses, engineers, nutritionists, social-service workers and others, and is equipped to assist physicians, boards of health and other agencies in solving problems connected with public health.

The location of these district officers and the names of the district health officers are as follows:

Southeastern District:

Dr. Harold W. Stevens
105 William Street, New Bedford
Tel. New Bedford 3-7081

South Metropolitan District:

Dr. Henry M. DeWolfe
1245 Hancock Street, Quincy
Tel. GRANite 5006

North Metropolitan District:

Dr. A. Daniel Rubenstein
519 State House, Boston
Tel. CAPitol 4600 (Line 312)

Northeastern District:

Dr. Robert E. Archibald
367 Main Street, Wakefield
Tel. CRYstal 1118

South Central District:

Dr. Oscar A. Dudley
476 Main Street, Worcester
Tel. Worcester 2-8805

North Central District:

Dr. Arthur E. Burke
Central Avenue, Ayer
Tel. Ayer 2305

Connecticut Valley District:

Dr. Walter W. Lee
278 Main Street, Greenfield
Tel. Greenfield 3061

Berkshire District:

Dr. Walter W. Lee
184 North Street, Pittsfield
Tel. Pittsfield 2-1929

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JULY, 1943

RÉSUMÉ

DISEASES	JULY 1943	JULY 1942	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	1	9	4
Chicken pox	398	436	402
Diphtheria	7	21	14
Dog bite	1150	1227	1199
Dysentery, bacillary	2	0	11
German measles	469	212	60
Gonorrhea	355	413	389
Measles	1468	1159	1159
Meningitis, meningococcal	62	13	5
Meningitis, other forms	7	7	•
Meningitis, undetermined	3	0	431
Mumps	244	555	155
Pneumonia, lobar	93	100	9
Salmonella infections	19	9	257
Scarlet fever	440	330	424
Syphilis	363	427	292
Tuberculosis, pulmonary	214	314	28
Tuberculosis, other forms	19	22	4
Typhoid fever	6	4	521
Undulant fever	7	4	
Whooping cough	317	882	

*Pfeiffer-bacillus meningitis only other form reportable previous to 1941

COMMENT

The outstanding feature of the July communicable disease picture is the poliomyelitis figure, with only 1 case reported for the month; hence the chances of a sizable outbreak seem rather remote. Incidentally, this is the lowest number of recorded cases for July so far as this disease is concerned. Meningococcus meningitis, although still at a point twelve times as high as that of the seven-year median, has experienced a 33 per cent drop since June. Scarlet fever, which reached epidemic proportions during the previous months, is now well on its way down to more satisfactory levels.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Wakefield, 1; total, 1.

Diphtheria was reported from Boston, 1, Cambridge, 1, Dennis, 1, Everett, 1, Fall River, 2, Woburn, 1, total, 7

Dysentery, bacillary, was reported from Boston, 2 total, 2

Encephalitis, infectious, was reported from Barnstable 1, Brockton, 1, Cambridge, 1, Everett, 1, total, 4

Malaria was reported from Camp Edwards, 1, Fort Banks, 6, Fort Devens, 4, Millbury, 1, Whately, 1, total, 13

Meningitis, meningococcal, was reported from Ashland 1, Auburn, 1, Barnstable, 1, Boston, 16, Bourne, 1, Brookline, 1, Cambridge, 3, Camp Edwards, 2, Canton 1, Fall River, 3, Fitchburg, 1, Fort Banks, 1, Fort Devens, 2, Haverhill, 3, Holyoke, 3, Longmeadow, 1, Lowell, 1, Lynn, 1, Malden, 2, Methuen, 2, Pittsfield, 2, Quincy, 1, Rockland, 1, Somerville, 1, Springfield, 2, Stoneham 1, Templeton, 1, Wakefield, 1, Watertown, 1, Weymouth, 1, Wilmington, 1, Worcester, 2, total, 62

Meningitis, other forms, was reported from Boston 3, Chelsea, 1, Fall River, 1, Melrose, 2, total, 7

Meningitis, undetermined, was reported from Braintree, 1, Cambridge, 1, Worcester, 1, total, 3

Salmonella infections were reported from Boston, 2, Braintree, 1, Brookline, 2, Cambridge, 1, Grafton 1, Lawrence, 2, Methuen, 1, Norwood, 1, Peabody, 2, Pittsfield 1, Salem, 4, Spencer, 1, total, 19

Septic sore throat was reported from Beverly, 1, Boston, 5, Williamstown, 1, total, 7

Tetanus was reported from Brockton, 1, total, 1

Trachoma was reported from Boston, 1, total, 1

Trichinosis was reported from Boston, 2, Dover 1 total, 3

Tularemia was reported from Falmouth, 1, Walham, 1, total, 2

Typhoid fever was reported from Boston, 1, Fall River, 1, Holyoke, 1, North Attleboro, 1, Salisbury, 1, Saugus, 1, total, 6

Undulant fever was reported from Adams, 1, Boston 1, Gloucester, 1, Hawley, 1, Merrimac, 1, Spencer 1, Sudbury, 1, total, 7

BOOK REVIEWS

Changes in the Knee Joint at Various Ages with Particular Reference to the Nature and Development of Degenerative Joint Disease By Granville A. Bennett, MD, Hans Waane, MD, and Walter Bauer, MD 4°, cloth, 128 pp., with 9 illustrations and 31 plates New York: The Commonwealth Fund, 1942 \$2.50

As the authors state in their preface, the rheumatic disorders rank foremost among the crippling diseases and are a frequent cause of prolonged morbidity. The origin and exact characteristics of these disorders are imperfectly understood. Barring the chance discovery of a specific substance or some special method of treatment, it seems that the most promising approach to the problems that these disorders present is the one chosen by the authors. It is a fundamental necessity to know what goes on in apparently normal joints as age advances before one can even make shrewd guesses concerning the exact causes and the exact nature of the pathologic changes that are responsible for abnormal joints affected by any chronic progressive disease of uncertain etiology. The authors of this clearly written and beautifully printed and illustrated volume speak with authority de-

rived from a complete familiarity with the extensive literature of the rheumatic disorders for the last one hundred years, a sound pathological training and a long clinical experience in the treatment of these disorders.

Investigation of the changes in the human knee joint at various ages was initiated by Bauer and Bennett in 1933. Their purpose was to familiarize themselves with the appearance of and the changes in the so-called normal joint as life goes on by studying these joints at each decade of life. The material was obtained post mortem or from amputations and was limited to those joints in which, so far as they could establish the fact, there had been no history or clinical evidence of arthritic disease. They found that all the joints obtained from individuals beyond the second decade of life exhibited alterations similar to those observed in hypertrophic arthritis (degenerative joint disease). The authors concluded that the articulations remain normal for only a very short time after maturation. They state 'Why this is so remains a riddle, as does the whole process of aging. Because of the wide distribution of degenerative joint disease, it is evident that the disease is not climatically limited nor confined to the human species.'

Their material consisted of sixty three knee joints from persons ranging in age from one month to ninety years. In none of these joints in life had there been any symptoms of joint disease, and no abnormalities had been noted in clinical examinations. However, in every subject beyond the age of fifteen some degeneration was found in one or more tissues of the joints.

In the sixth decade the loss of all articular cartilage from an eburnated epiphysis was observed. Apparently the degree of villous hypertrophy and of synovial fibrosis was not proportional to the degree of change in the cartilaginous surfaces of the joints. In several specimens the synovial membranes were practically normal. In the seventh decade it was rare to find any one of the articular structures entirely normal. Typical marginal lipping was very frequent and the semilunar cartilages were badly damaged. In the eighth decade large areas of complete absence of articular cartilage were found on the weight bearing surfaces of the femur and of the tibia. These changes were still out of proportion to the changes in the synovial membrane but the semilunar cartilages showed more fraying and partial calcification. In the ninth and tenth decades all these changes were more advanced.

Chapter IV, in which the authors give their interpretation of these articular findings, does not lend itself to abstract and should be read in toto. It is evident that they have become convinced that the reparative powers of hyaline articular cartilage are extremely limited and that if necrosis occurs it is replaced by imperfectly formed fibrocartilage. The subchondral bone suffers in like manner and concomitantly with the articular cartilage.

In Chapter V the authors' concepts of pathogenesis are given. They were arrived at not only as a result of this detailed visual study of the changes in normal joints but from their previous sound research work and their wide clinical experience. The authors appear to have assumed an entirely dispassionate attitude which is admirable and rather rare. They have presented the evidence and carefully weighed its value especially in relation to etiology. It is unfortunate that war service has made it temporarily

impossible for this brilliant teamwork to follow closely the elusive but fresh scent that certain unpublished research has already provided.

The Biological Action of the Vitamins. A symposium edited by E. A. Evans, Jr., Ph.D. 8°, cloth, 227 pp., with 36 illustrations and 8 tables. Chicago: The University Press, 1942. \$3.00.

This is an outstanding collection of papers on recent fundamental investigations regarding the vitamins. The fourteen contributions included were presented at the University of Chicago in September, 1941, in co-operation with the University of Wisconsin, and a like symposium was given at Madison on respiratory enzymes. The volume contains papers on the biologic action of the vitamins in general, including cocarboxylase, thiamine, riboflavin, nicotinic acid, pyridoxine, pantothenic acid, biotin and vitamin K. The contributors include some of the most eminent workers in their fields, notably C. A. Elvehjem, Paul György, Norman Jolliffe, D. W. MacCorquodale and Vincent du Vigneaud.

In general outlook these papers consider not only the chemistry of the vitamins and their relation to experimental and clinical deficiency states, but also their rapidly unfolding roles in the field of the respiratory enzymes, in carbohydrate metabolism and in promoting the growth of yeasts and bacteria. For example, they point out that riboflavin is a prosthetic group in coenzyme II, which aids in catalyzing the oxidation of hexose monophosphate, and that it is essential for the growth of lactic acid bacteria; that the enzyme cocarboxylase, concerned in the decarboxylation of alpha keto acids, is an ester of thiamine; and that biotin has been found identical with coenzyme R, a compound necessary for the growth of certain nitrogen-fixing bacteria, and also with protective factor X or vitamin H, which inhibits the harmful effects of feeding raw egg white to certain animals.

Perhaps the most fascinating paper is that of du Vigneaud on biotin, which recounts the most recent chemical triumph in the field of vitamins. All are well worth reading, however, and this book is highly to be recommended.

The Hemorrhagic Diseases and the Physiology of Hemostasis. By Armand J. Quick, Ph.D., M.D. 8°, cloth, 340 pp., with 24 illustrations and 9 tables. Springfield, Illinois: Charles C Thomas, 1942. \$5.00.

The past five years have witnessed great clarification in the mysteries surrounding the various problems relating to blood clotting. In this period a number of seemingly unrelated investigations have converged: new knowledge regarding prothrombin and methods for its detection, the discovery of the antihemorrhagic vitamin K, the purification and therapeutic use of heparin, and the discovery in sweet-clover disease of cattle of the hemorrhagic factor dicoumarol. In these investigations the name of Quick has constantly loomed large, and it is therefore fitting that the first authoritative monograph on the physiology and clinical manifestations of normal and abnormal hemostasis should have been written by this Marquette University investigator.

The book is distinguished by its thoroughness and clarity, and above all by its wisdom. Well and simply written, it fulfills a long-felt need in grouping together in separate chapters the many accumulated bits of knowl-

edge regarding thrombin, prothrombin, thromboplastin, fibrinogen, platelets and anticoagulants. The references, which are unusually complete, are alphabetically grouped at the end of each chapter.

Discussions of physiologic principles are followed by chapters dealing with such clinical conditions as thrombopenic purpura, hemophilia and hypoprothrombinemia, and with the uses of heparin and dicoumarol. Although a thorough discussion and painstaking review of the literature distinguish these chapters, they suffer somewhat from the author's primary concern with the laboratory rather than with the clinic. Particularly with thrombopenic purpura and hemophilia there is too much reliance on the literature and on some of the author's "pet" theories, for example, a histamine disturbance in purpura and a simple thromboplastin defect in hemophilia. There is increasing evidence that idiopathic thrombopenic purpura is primarily a splenic dysfunction with remote, possibly hormonal, inhibition of platelet formation from megakaryocytes in the bone marrow. As regards hemophilia, the clearcut experiments of F. H. L. Taylor and his associates at the Thorndike Memorial Laboratory of the Boston City Hospital are dismissed with scant notice. Whether hemophilia is primarily a thromboplastin deficiency or an abnormality in the euglobulin fraction of the plasma is still not entirely settled; perhaps both groups of investigators are correct.

These criticisms are possibly captious, for the book is not only authoritative and thorough but respectful of the extensive literature and not unmindful of the historical roots of each particular subject. The format, typography and printing are quite in keeping with the general excellence of the work, which is completed by an appendix containing methods for determination of the coagulation time, bleeding time, clot retraction, platelet count, and levels of prothrombin and fibrinogen, together with methods for the assay of thromboplastin, thrombin and heparin.

The book is highly recommended for use in general hospitals and clinical laboratories. Collaboration with a clinical investigator might be desirable in a second edition.

First Aid to the Injured and Sick: An advanced ambulance handbook. Edited by Major Norman Hammer, M.R.C.S. Eighteenth edition. 16°, paper, 336 pp., with 313 illustrations. Baltimore: The Williams and Wilkins Company, 1941. \$2.00.

The fact that this little volume is its eighteenth edition speaks well for its popularity. The first part of the book is devoted to the form and functions of the body. This section gives a clear and remarkably well-illustrated account of body structures in an extremely simple and concise manner.

The author states that air-raid first aid has been his special interest for the past five years, and the numerous illustrations of and directions for first aid show how well he has accomplished his task of explaining sound methods clearly and graphically to the students of this subject. The chapter on sprains, dislocations and fractures is particularly commended, as is the section on the first-aid treatment of hemorrhage and wounds. The newer treatments of burns and injuries from gassing are given careful attention.

The book will be of great value to all who would familiarize themselves with first-aid treatment.

(Notices on page x)

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ACUTE PERICARDITIS WITH SPECIAL REFERENCE TO CHANGES IN HEART SIZE*

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THE 5 cases that form the basis of this report have certain features in common. The patients were young or middle aged men with normal hearts. During an acute respiratory infection acute pericarditis supervened. The most remarkable feature was a rapid, conspicuous enlargement in the size of the heart, followed by a slower reversion toward normal and recovery without any demonstrable cardiac abnormality. Similar cases have been seen but are not included in this report because in them the opportunity for x-ray confirmation of heart size was not available.

Of particular interest at the present time are 3 cases in which the pericarditis complicated atypical primary pneumonia.

CASE REPORTS

CASE 1. L. R., a 37 year old, married man, with negative family and marital histories, entered the Beth Israel Hospital for the third time on September 19, 1929. The past history was negative except for thyrotoxicosis. During each of the previous two admissions (December 1928 and March, 1929), subtotal thyroidectomy was performed for hyperthyroidism. The patient had had repeated paroxysms of auricular fibrillation, but there was no demonstrable structural abnormality of the heart by physical, roentgenographic or electrocardiographic examination. The blood pressure was normal. Following the second thyroidectomy he gained weight and felt well enough to return to work. However, the basal metabolic rate remained elevated, so that he was given Lugol's solution, and just prior to the third admission was subjected to three weekly roentgen-ray exposures over the thyroid gland, the basal metabolic rate being +18 per cent. The patient was readmitted several days after the onset of pain in the neck and across the upper chest, stiffness of all the muscles and general malaise. Examination on admission revealed slight injection of the pharynx, auricular fibrillation and fever.

The temperature varied between 98° and 102°F until the 37th day after admission, remaining normal thereafter.

except as noted below. The pulse showed marked fluctuations, due to frequent short paroxysms of auricular fibrillation. The respirations averaged 20. During the febrile period general malaise, slight cough, a feeling of substernal constriction, sharp precordial pain and anorexia were the outstanding symptoms. The physical signs in the lungs were variable, consisting of slight dullness, diminished breath sounds and fremitus at the right base crepi-



FIGURE 1. Case 1 (September 27, 1929)

This film shows considerable enlargement of the heart shadow compared with that in a previous film. Normal cardiac landmarks are preserved.

tant rales under the angle of the right scapula and a pleural friction rub in the right axilla. Examination of the heart on admission revealed no abnormalities except in rhythm, but from the 22nd to 38th hospital days a pericardial friction rub was constantly audible over the entire precordium. It was not possible to demonstrate Kussmaul's sign, and distended neck veins, evidence of a congested

*Thyroid and all subsequent figures are reported on x-ray films taken at a distance of seven feet. They were reproduced to show the cardiac outline as clearly as possible without regard for the details of the pulmonary lesions.

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liver, edema and blood pressure changes were not observed.

On the 57th day, the patient having recovered from the acute illness, thyroidectomy was performed for the third time. Convalescence was uneventful except for the re-



FIGURE 2. Case 1 (December 10, 1929).

The heart size is normal, and the configuration and measurements are identical with those in films taken prior to this patient's illness and subsequent to his recovery, a period of thirteen years.

currence of the precordial pain, the pericardial friction rub and a temperature of 102°F. on the 74th day. The patient was discharged in excellent condition 9 days later.

The hemoglobin level and red-cell count were 85 per cent and 4,090,000, respectively. The white-cell counts varied between 6800 and 14,600 but were usually normal. Five vital-capacity determinations ranged between 2450 and 2800 cc. Teleroentgenographic measurements showed a total transverse diameter of 17 cm. on the 8th day (Fig. 1), and 14.2 cm. on the 82nd day (Fig. 2), the internal diameter of the chest being 28.5 cm. on both occasions. There was diminished radiance of both lung bases, especially on the right, and slight haziness in the right costophrenic angle. An electrocardiogram on admission showed auricular fibrillation and normal RST segments and T waves. Four days later, the RST segments were displaced upward in Leads 1 and 2, and the ascending limb of the T waves rose in a straight line; T₃ was inverted. All subsequent electrocardiograms displayed inverted T waves in all leads.

The patient developed diabetes in 1930, requiring insulin. Paroxysms of auricular fibrillation continued, but there was no demonstrable structural abnormality of the heart. Electrocardiograms and x-ray examinations were identical to those taken prior to the third hospital admission. He was last seen in 1942.

CASE 2. J. M., a 50-year-old pharmacist, entered the Beth Israel Hospital on January 29, 1941, and was discharged on February 12. His father died of cancer of the bowel, his mother of diabetes. Two sisters had diabetes, and four sisters and one brother were living and well. The marital and past histories were irrelevant.

The present illness began 12 days before entry with a feeling of malaise and feverishness. Finding his temperature elevated, the patient immediately went to bed. His physician found a few rales at both lung bases, a normal heart and a temperature of 100°F. Five days before entry, a pericardial friction rub was heard for the first time, and 2 days before entry the temperature rose to 102°F, after which it remained normal until entry. There was no chest pain at any time. The patient perspired a great deal and had an occasional dry cough. A diagnosis of bronchopneumonia was made.

The temperature on admission was 100.4°F. (rectal), rising to 101 on the 2nd day, after which it was normal. The pulse was 100 and respirations 22. The blood pressure was 120/80. A few fine crepitant rales were heard at both lung bases. A loud pericardial friction rub was audible all over the precordium, and persisted until January 30.

The hemoglobin level and red-cell count were normal. Three white-cell counts were 12,200, 7500 and 6600. A tuberculin skin test was positive in a dilution of 1:10,000.



FIGURE 3. Case 2 (January 29, 1941).

There is considerable cardiac enlargement, especially to the left. The silhouette is not suggestive of effusion, and the normal landmarks are preserved. The pulsations observed under fluoroscopic screen were of fan amplitude.

Sputum examinations for tubercle bacilli were negative. The corrected sedimentation rates were 2.3, 1.9, 1.1 and 0.7 mm.

A teleroentgenogram taken on the day of admission (Fig. 3) showed the total transverse diameter of the heart to be 15.8 cm. The roentgenologist reported the pulsations to be of fair quality, and there was no evidence of pericardial fluid. On February 10, the total transverse diameter of the heart was 13.5 cm. (Fig. 4).

Electrocardiograms showed the typical changes of acute fibrinous pericarditis; the last one, taken on February 11, still showed inverted T waves in Leads 2 and 3, but the T waves in Leads 1 and 4 had become upright. One month after discharge all leads were normal.

CASE 3. H. W., a 23-year-old man, was seen at home on July 29, 1933. He had never been robust, but led an active life and worked hard. Three years previously he had had a carbuncle on the upper lip. There was a history of diabetes in the mother and of rheumatic heart

was held tensely. The blood pressure was 120/70. The temperature fluctuated between 98 and 103°F. for the first 3 days, and was normal thereafter.

The white cell count on admission was 19,800, rising to 23,800 on the following day, and thereafter quickly falling to a normal level. Two blood cultures were negative. Electrocardiograms revealed the classic pattern of early acute fibrinous pericarditis.

The roentgenologist's report is of particular interest. There was a remarkable change in the size of the heart in 9 days, with an increase of 2.4 cm. Pulsations of the heart were fairly distinct, but the shape of the heart was that of pericardial effusion. There was no evidence of undrained fluid in the left pleural cavity or new areas of dullness in either lung. The diaphragm moved fairly well on both sides.

Although there was no clinical evidence of pericardial effusion, several pericardial taps were attempted, yielding 1 cc. of sanguineous fluid, which proved negative on culture. By the 10th hospital day the heart size had returned to normal, and the patient was discharged. He has remained completely well to the present time.

CASE 4. S. B., a 30-year-old, married man, was seen in another hospital on September 19, 1942. The present ill-



FIGURE 4. Case 2 (February 10, 1941).

The heart size is within normal limits. The silhouette corresponds to that seen in Figure 3.

disease in a brother. The present illness began 6 days before the first examination, with a slight unproductive cough and precordial pain. Three days later the patient felt chilly and the temperature rose to 101°F., reaching 102 on the following day. An insect bite above the right eye, sustained a week before, resulted in a purulent discharge, but this rapidly healed.

Examination showed consolidation of the left lower lobe. The heart and blood pressure were normal. On August 4, the signs were suggestive of fluid at the left base. From August 2 until admission to a hospital on August 8, a loud pericardial friction rub was constantly audible over the entire precordial area.

The white-cell count on admission was 25,400, falling gradually to 8700. X-ray examination of the chest disclosed fluid in the left pleural cavity, displacing the heart to the right.

A trocar thoracotomy was performed on the 2nd hospital day, and a free flow of pus was obtained. Culture yielded a pure growth of *Staphylococcus aureus*. The temperature fell sharply, but throughout the rest of the hospital stay there were slight rises above normal. X-ray films of the chest showed considerable improvement, and the patient was discharged on August 31, completely relieved except for slight pain in the left shoulder.

Two days later severe, sharp precordial pain recurred, followed in 2 or 3 days by sharp pain in both axillae, feverishness and profuse sweating. The patient remained up and about, but was readmitted 5 days following his discharge.

Examination revealed increased cardiac dullness, both to the right and to the left. The cardiac impulse was easily identified, and was not forceful but rather diffuse. The rate was rapid and the sounds were vigorous. There was a pleural friction rub at the left base. The abdomen



FIGURE 5. Case 4 (September 19, 1942).

The heart shadow is considerably enlarged, which is suggestive of pericardial effusion.

ness began on September 5 with headache, slight cough, profuse sweating, feverishness and generalized aching. When the patient was seen by his physician 5 days later the headache was still severe and the cough was unproductive and harassing. There were small pin-point areas of inflammation in the throat and crepitant rales in both lungs. The heart was normal. The patient was examined every day from then on, nothing unusual being found in the heart. On September 18 he felt well enough to shave himself. At 1:30 a.m. on the following day he was awakened by sharp precordial pain and a constricting pain in the anterior chest of great severity, requiring morphine. A pericardial friction rub was heard a few hours later. On arrival at the hospital an x-ray film was taken (Fig. 5), which showed considerable car-

diac enlargement. The white-cell count was normal and the temperature was 101°F.

Physical examination showed a well-looking young man in no apparent discomfort, but complaining of occasional precordial pain. The area of cardiac dullness was increased. The palpable cardiac impulse was diffuse and corresponded with the left border of dullness. The rate was moderately rapid and the rhythm regular. A loud pericardial friction rub was audible over the entire precordial area. The heart sounds were distinctly and easily heard but were of rather poor quality. The only pulmonary finding was diminished respiratory excursion of the left lower chest. The blood pressure was 142/76. The pulse was of good quality; a paradoxical pulse could not be demonstrated. There was no distention of neck veins or liver, no Ewart sign and no edema or respiratory embarrassment.

Daily swings in temperature up to 104°F. were recorded until October 1, after which the temperature remained normal. The pulse averaged 85 and respirations

ber 21. At no time was there dysphagia. Three weeks later there were no abnormal physical findings and the blood pressure was 142/90.

The white-cell count was normal except on September 20, when it reached 14,300, thereafter rapidly return-



FIGURE 6. Case 4 (October 2, 1942).

There is still considerable enlargement of the heart shadow, but the landmarks are visible, and there is no suggestion of pericardial effusion.

20. Sulfadiazine was administered in adequate doses both before and after admission, but no benefit resulted and the drug was therefore discontinued. By September 22, the heart sounds had considerably improved, but the size of the heart was unchanged. The friction rub remained loud over the entire precordium until October 2, when it was limited to the region of the aortic valve. At that time the heart was much smaller (Fig. 6). An x-ray film taken on October 16 (Fig. 7) showed that the heart size was almost within normal limits. The blood pressure remained unaltered during the entire illness, and at no time were clinical signs of pericardial effusion elicited. Slight dullness and rales at both lung bases appeared, and finally a small area of bronchial breathing with increased spoken voice at the right base was detected. The cough gradually subsided, and the patient was well enough to leave the hospital on Octo-



FIGURE 7. Case 4 (October 16, 1942).

The heart size is almost within normal limits. Comparison of the supracardiac shadow with that in Figure 5 shows an almost identical contour in both instances, indicating that, if fluid was present early in the course of the disease, the amount was very small.

ing to normal. Several electrocardiograms showed the characteristic pattern of acute fibrinous pericarditis. An electrocardiogram on November 14 revealed entirely normal curves.

CASE 5.* A.R., a 42-year-old, married salesman, entered the Beth Israel Hospital on August 21, 1942. The past history was negative except for tonsillectomy 25 years previously and influenza 24 years previously. The mother had hypertension.

The present illness began 2 weeks before admission with the onset of diarrhea, which lasted for 3 days. The patient continued to work as a traveling salesman, but 1 or 2 days after the diarrhea stopped he noted general malaise, loss of appetite and feverishness, and several days later a nonproductive cough. His physician made a diagnosis of "grippe" and advised rest in bed. The temperature fluctuated from normal to 103°F. up to the time of admission. The cough became progressively worse.

On August 21, the patient complained of stabbing precordial pain and sharp pain in the right anterior chest, aggravated by inspiration and causing some difficulty in breathing. He became aware of sudden rapid beating of the heart, together with great weakness. The family physician was unable to measure the blood pressure, and sent him to the hospital after administering morphine and Paredrine.

*Reported through the courtesy of Dr. Hyman Morrison.

Physical examination revealed a cold and clammy skin, respiratory difficulty owing to pleuritic pain, slight cyanosis and marked weakness. The temperature was 103°F (rectal), the heart rate 214 (electrocardiogram), and the respirations 24. The posterior pharyngeal wall was in

was of a normal pattern, and a teleroentgenogram (Fig 9) showed the heart to be of normal size and the lung fields clear.

CAUSE OF THE CHANGES IN HEART SIZE

The differential diagnosis between dilatation of the heart and pericardial effusion is, as most clinicians agree, often a difficult and sometimes an insoluble problem. It is necessary to consider all the information obtained by examination of the heart and chest, a general and detailed study of the circulation, x-ray examination and fluoroscopy, electrocardiography and paracentesis. No one of these methods, including paracentesis, is infallible,

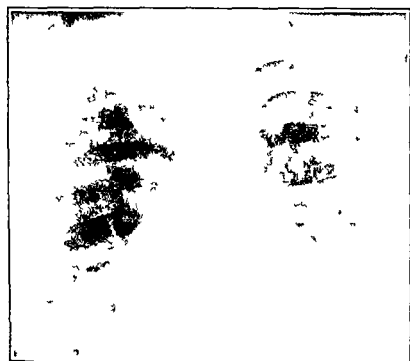


FIGURE 8 Case 5 (August 26 1942)

There is considerable increase of the heart size. The normal landmarks are preserved, and there is nothing to suggest effusion.



FIGURE 9 Case 5 (December 5 1942)

This shows a normal cardiac silhouette. The general contour is similar to that in Figure 8.

jected. The heart appeared to be enlarged and extremely rapid and the sounds were of poor quality. There were scattered crepitant rales over both lung bases, but no areas of dullness and no bronchial breathing or other abnormal signs. The examination was otherwise negative.

The white-cell count on admission was 15,000, rising to 16,400 on the 4th hospital day and falling to 12,000 on the day of discharge. A heart film taken on August 26 (Fig 8) showed enlargement of the heart and a pneumonic process at the right base.

The admission electrocardiogram showed a supraventricular type of tachycardia with a rate of 214. There was slight elevation of the RST segment in Leads 2, 3 and 4 without any displacement in Lead 1. The following day the rhythm was normal, and the rate 105; there was slight inversion of T_1 , and the RST segments were still elevated in Leads 2, 3 and 4, with an upper concavity of the ascending limb of the T waves. The final electrocardiogram, taken the day before discharge, showed inverted T waves in all four leads.

Three tenths of a gram of quinine hydrochloride was injected intramuscularly on admission, and $2\frac{1}{2}$ hours later the heart rate was 100. The blood pressure was unobtainable at first, but rose slowly to 110/80 after the restoration of normal rhythm. Clinical improvement was rapid in spite of the continuance of cough, but the rales at the bases increased, and slight dullness to percussion and suppressed breath sounds appeared over the right base. After the 3rd hospital day the temperature remained normal, and on the 8th day the patient insisted on going home.

He was next seen on December 5. Recovery was complete. The patient was working full time and attending gymnasium twice a week. Examination revealed no abnormalities of the heart or lungs, the electrocardiogram

but the collective data obtained by all of them may permit an accurate evaluation.

Nowadays, few clinicians cling to the idea that the presence of a pericardial friction rub is incompatible with an effusion in the pericardial sac. The location and distribution of the rub, however, is of some significance, since in most cases when excess fluid accumulates in the pericardial cavity the friction sound disappears in the region of the apex while persisting over the base of the heart and sternum.

The heart sounds are much more apt to be muffled, distant or absent in cases of effusion than in cases of dilatation, although in the latter the quality of the sounds may change and gallop rhythm may be present.

Increase in the area of absolute dullness on percussion may be striking in cases of pericardial effusion, and the abrupt transition from absolute dullness to normal resonance may help in the diagnosis. The area of supracardiac dullness may be increased.¹

A paradoxical pulse is often found when fluid is present.

The cardiac impulse is usually absent when the pericardial sac contains a large amount of fluid, but is not obliterated in cases of cardiac dilatation. In the latter it may be noted as a diffuse, wavy impulse, and with few exceptions the left border of cardiac dullness corresponds to it. Should the cardiac impulse be detectable in a case of effusion, the left border of dullness may extend far to the left and below its location.

There has been considerable controversy regarding the presence and significance of physical signs over the posterior aspects of the lungs in pericardial effusion.² These signs include almost all those known to occur, but whether they correspond to those described by Bamberger-Ewart or present some less characteristic pattern, or are similar to the findings in pleural effusion, most observers agree that they are indicative of fluid in the pericardial cavity. Such signs may be elicited on the right as well as on the left side, or may be limited to the right side. In evaluating signs that are suggestive of pleural effusion, the latter may be excluded by x-ray examination. Posterior signs are never produced by heart enlargement alone.

Dilatation of the heart may occur without necessarily resulting in circulatory disturbances. It is well known, however, that pericardial effusion, even when not large, may cause profound alterations in the circulation. Dyspnea, cyanosis, markedly distended neck veins, a fall in arterial blood pressure with decreasing pulse pressure, a rise in venous pressure, an acutely distended and depressed liver and so forth are too well known to require comment. Yet in some cases large collections of fluid are compatible with an apparently normal circulation. The critical factor is the speed with which fluid accumulates in the pericardial sac.³⁻⁶

Reliance on x-ray examination in the differentiation of cardiac dilatation from pericardial effusion has been the cause of many errors in diagnosis. Nevertheless, this method of examination is of considerable value. The water-bottle configuration is not conclusive evidence of fluid and may be seen in cases of dilatation. The absence of pulsations on fluoroscopy may indicate fluid, but feeble pulsations may be misleading. Vigorous pulsation of the aortic knob and decreased pulsation of the left ventricular border suggest fluid (Freedman⁷). This author is also of the opinion that the most reliable diagnostic procedure is daily roentgen-ray examination of the heart. The finding of considerable change in its size within short periods of time he considers the best sign of fluid. A change in the outline of the cardiac silhouette with a change in position of the patient has been stressed by many observers.

Low voltage in the electrogram may be found when excess fluid is present.

The vital capacity is diminished with effusion.²

The final proof of the existence of excess fluid depends on its actual demonstration by paracentesis, operation or autopsy. The failure to withdraw fluid with a needle does not prove its absence, for fluid may be encapsulated or the technic of paracentesis may be at fault.

The differential diagnosis between pericardial effusion and cardiac dilatation was carefully considered in each case in this series, and since the primary purpose of this paper is to report the rapid enlargement of the heart in acute fibrinous pericarditis, it will be necessary to state the reason for considering the change in heart size as due to dilatation, and not to effusion in the pericardial cavity.

In Case 1, the first evidence of pericarditis was furnished by the electrocardiogram. The pattern observed was pathognomonic of early acute pericarditis, so that the diagnosis could be made with confidence in the absence of other evidence.⁸ Four days later a teleroentgenogram (Fig. 1) showed a great increase in the size of the heart compared to the previous plate, in which the measurements were within normal limits. The configuration of the heart shadow was not considered to be at all suggestive of effusion; the normal landmarks were preserved. An increase of such magnitude in so short a time, if due to effusion would in all probability have given rise to clinical manifestations of circulatory embarrassment. Yet these were singularly absent and the vital capacity was constant throughout the illness. The heart sounds remained normal; the friction rub during the period of its audibility, could be heard at the apex, and there was a complete absence of characteristic posterior lung signs, distended neck veins, an enlarged tender liver, a change in blood pressure and so forth.

The diagnosis of pericarditis in Case 2 was first made on the basis of a friction rub. Five days later a teleroentgenogram (Fig. 3) showed considerable cardiac enlargement. The heart contour was not suggestive of fluid, and under the fluoroscope the cardiac pulsations were seen to be of fair amplitude. As in the previous case, there were none of the numerous signs or symptoms that are associated with a large or rapidly accumulating pericardial effusion. A second teleroentgenogram (Fig. 4), taken twelve days after the first one, showed the heart measurements to be within normal limits, and the total transverse diameter had decreased 2.3 cm.

In Case 3, the roentgenologist was so impressed by the remarkable increase in heart size in nine days that, although the cardiac pulsations were

distinct, it was his opinion that pericardial effusion was present. The electrocardiogram was pathognomonic of early acute fibrinous pericarditis. Clinically the heart was enlarged to the right and to the left. The cardiac impulse was easily felt and was not forceful but rather diffuse. The heart sounds were loud and there were no signs of compression. Nevertheless, in view of the recent empyema, the roentgenologist's opinion and the high white-cell count, several pericardial taps were attempted, but no fluid was found.

The cardiac silhouette in Case 4 suggested the presence of pericardial fluid. However, if it was present the amount was very small and was responsible for but little enlargement of the cardiac shadow. The teleroentgenogram taken several hours after the onset of pericarditis (Fig. 5) revealed a degree of enlargement that, if due entirely or for the most part to effusion, indicated an extremely rapid accumulation of fluid. This would in all probability have given rise to obvious circulatory disturbances. After seeing the x-ray film, every attempt was made to elicit clinical symptoms or signs of effusion, but these were consistently absent. The increase in cardiac dullness was inconspicuous, the apex impulse remained palpable, the friction rub was constantly audible over the apex of the heart as well as over the base, there was no change in cardiac outline with change of position, and the heart sounds were good. As the size of the heart decreased, even though there was still considerable enlargement, the contour no longer suggested the presence of fluid (Figs. 6 and 7).

The diagnosis of pericarditis in Case 5 was made solely on the basis of the electrocardiograms. The first two showed RST elevations without reciprocal depressions, and without changes in the QRS waves, which may be considered pathognomonic of early acute pericarditis. The third electrocardiogram showed inverted T waves in all the leads. The first x-ray film (Fig. 8) was taken five days after the onset of pericarditis and showed considerable enlargement of the heart without any of the features that are helpful in making a diagnosis of pericardial effusion. Clinically, as in the cases cited above, there was nothing to indicate a rapidly forming effusion.

In none of the cases was a decrease in amplitude of the QRS waves in the electrocardiogram, such as may be seen with pericardial effusion, observed.

The opinion appears warranted, in all these cases, that the rapid and striking increase in the size of the contents of the pericardial sac was due to an increase in the size of the heart itself and not to an increase of pericardial fluid. It is unlikely that fibrin deposits could have contrib-

uted materially to the rapid and striking changes in size that were seen. The same may be said in regard to swelling or edema or diffuse inflammatory infiltration of the heart muscle, particularly in view of the fact that circulatory efficiency did not appear to be impaired in the slightest degree. Simple dilatation of the heart, it would seem, was responsible for the phenomenon observed. Yet these patients appeared to be extremely well, and in none of them were symptoms or signs of circulatory disturbances observed.

MECHANISM OF ACUTE DILATATION

The anatomical structure of the pericardium and its ligaments¹⁰ suggests that one of its functions is to restrain dilatation of the heart. Although there is no uniformity of opinion concerning this point, most of the clinical and experimental evidence favors this view.¹¹⁻²⁶ If one were to ascribe the dilatation observed in our cases to pericarditis alone, it would be necessary to assume that the restraining function of the pericardium is lost when pericarditis occurs. There is no evidence to support this assumption; dilatation, moreover, does not occur in all cases of pericarditis. In suppurative pericarditis and in tuberculosis, a small heart is the rule. But in these two conditions an outpouring of fluid takes place that, together with the pericardium, which has yielded to the maximum extent conditioned by the inflammatory process and effusion, acts to restrain cardiac dilatation. It appears that in some cases, when the pericardium is inflamed, either effusion or cardiac dilatation follows.

It has been shown that, when the characteristic electrocardiographic pattern of acute pericarditis occurs, diffuse subepicardial myocarditis is present.^{8, 9, 27-29} Since this pattern was observed in our cases, the additional factor of myocardial inflammation in causing dilatation must be considered.

Finally, the relatively slow heart rate, sinus arrhythmia and paroxysmal auricular fibrillation observed in our cases suggest that preponderant vagal tone may occur in the presence of pericardial inflammation and act as additional factors favoring cardiac dilatation. Van Liere and Crisler²⁶ have shown experimentally that vagal stimulation causes dilatation of the heart, and that the dilatation is greater, sometimes considerably so, if the pericardium is slit so that it loses its restraining function. Observations on the heart rhythm and electrocardiographic patterns following injection or removal of the stellate ganglions in dogs offer further suggestive evidence that the neurogenic mechanism may be disturbed following pericardial injury.⁸

The clinical evidence in the cases under discussion does not favor the view that impaired circulation in the pneumonic lung, anoxemia and toxemia were effective in producing cardiac dilatation.³⁰

It is possible that paroxysmal tachycardia in Case 5 played some part in producing cardiac dilatation. It should be noted, however, that the paroxysm lasted only a few hours, and that the teleroentgenogram showing enlargement was taken five days after the paroxysm had ended. Cardiac dilatation does not often occur as a result of tachycardia, even with rates approaching 200,³¹ and the available precise information³¹⁻³³ concerning the time of appearance of dilatation during paroxysmal tachycardia and its subsequent disappearance after the paroxysm has ended makes it extremely unlikely that the dilatation observed was related to the rapid heart action. Furthermore, in the accurately observed cases of dilatation associated with tachycardia, congestive failure was present; the cardiac silhouette, when the latter is present, may give a misleading impression of heart size.³⁴ These considerations make it even less likely that the paroxysms of auricular fibrillation had any bearing on the dilatation observed in Case 1.

Cardiac enlargement may occur in hyperthyroidism. In many if not all these cases, however, hypertension, coronary artery disease, valvular disease, congestive failure and so forth, are complicating factors.³⁵⁻³⁷ For these reasons, as well as the mildness of the hyperthyroidism and reversal of the heart size toward normal before the hyperthyroidism was corrected, thyroid disease is excluded as the cause of dilatation in Case 1.

DISCUSSION

Roentgenologic and orthodiagraphic demonstration of cardiac enlargement during acute infections has been reported by various observers.^{30, 38, 39} A careful search of the literature failed to disclose similar studies showing cardiac enlargement in acute pericarditis, such as occurred in the cases here reported. Aside from its interest as a feature of pericarditis, the importance of not mistaking the heart enlargement for pericardial effusion is obvious, as emphasized by Barnes and Burchell⁴⁰:

I have seen many cases of pericarditis in which the heart became large very rapidly, and I am convinced that in some of these cases we are dealing with the finest examples of acute dilatation of the heart which are known to clinical medicine. The enlargement is ordinarily ascribed to the accumulation of fluid in the pericardial sac, but I have had occasion to tap the pericardial sac as many as three times without obtaining any fluid whatsoever. Therefore, I believe that dilatation of the heart may occasionally be an important feature of acute pericarditis.

The clinical features of pericarditis were similar in all the cases. The pericarditis occurred in the course of an acute respiratory infection, having its onset after the first week, or in some cases when the original infection, which varied in severity from mild to severe, had about run its course. Evidence of active pericardial inflammation then persisted for as long as two or three weeks or, as in 1 case, for a much shorter time. A loud pericardial friction rub over the entire precordial area was usually audible during this entire period. Pericardial involvement was characterized by recurring sharp precordial pain, and in 2 cases by severe crushing anterior chest pain similar to that which occurs in acute myocardial infarction. Pleuritic pain was also usually present. The temperature chart may reveal but slight elevation, or a widely swinging temperature up to 104 or 105°F., while the pulse rate remains relatively slow and may show sinus arrhythmia. One patient had paroxysmal auricular fibrillation, and another paroxysmal auricular tachycardia. With the advent of pericarditis the white-cell count usually remains within normal limits or becomes slightly elevated. The corrected sedimentation rate is elevated. Once recovery sets in progress is rapid and without sequelae, and normal activity is soon possible. None of the patients have manifested residual cardiac defects; one of them has been followed for thirteen years, and another for nine years.

Cases 2, 4 and 5 occurred during a period when primary atypical pneumonia^{41, 42} was prevalent and was recognized and differentiated from the usual bacterial types of pneumonia. The clinical and x-ray features in these cases were similar to those described as occurring in primary atypical pneumonia, and the presence of ordinary bacterial agents could not be demonstrated. Although staphylococcal empyema was present in Case 3, the pulmonary infection was unlike the cases of staphylococcal pneumonia that have been described,^{43, 44} and its nature must remain in doubt. In this period (1933), 2 other cases of pericarditis that complicated pneumonia following a "grippe-like" infection were seen. The nature of the respiratory infection in Case 1 is also uncertain, except that the onset was like "grippe," which diagnosis, in fact, was originally made. The illness had none of the features suggesting that it might have been rheumatic carditis without valvular involvement.⁴⁵ Although pericarditis may occur as a postoperative complication,⁴⁶ including thyroidectomy,⁴⁷ the long lapse of time between thyroidectomy and the onset of pericarditis makes any causal relation extremely unlikely.

SUMMARY

Five cases of acute pericarditis complicating respiratory infections are described. In 3 cases the characteristics of the respiratory infection were similar to those occurring in primary atypical pneumonia.

Acute cardiac dilatation was demonstrated by teleroentgenograms and was unaccompanied by evidence of disturbed cardiac function. Complete cardiac recovery occurred in every case.

Acute cardiac dilatation is not identical with acute heart failure or with any symptoms or signs of altered cardiac function. Within certain limits of time and degree it may be regarded as physiologic.

The mechanism of acute cardiac dilatation associated with pericarditis is discussed.

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THE INTRAPERITONEAL USE OF SULFANILAMIDE IN GASTROINTESTINAL RESECTIONS

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THE present concept of the mode of action of the sulfonamide compounds provides a rational basis for their prophylactic intraperitoneal use in gastrointestinal surgery, and gives good reason to believe that this may be one of the most fruitful and advantageous fields for the employment of these drugs. A brief summary of the steps leading to the present knowledge of the action of these drugs will make clear the basis for this opinion.

Lockwood¹ in 1938 demonstrated that peptones resulting from the proteolytic action of bacteria exercise an inhibitory effect on the action of sulfanilamide, and suggested that the latter prevents the specialized metabolic activity required of invasive organisms. He offered evidence that this effect may be achieved by the prevention of utilization of protein metabolites by the organism. Fildes,² in a study of the mechanism of the antibacterial action of mercury, found that it is specifically neutralized by sulfhydryl (SH) compounds and concluded that mercury combines with them, thus depriving the bacteria of SH groups. This conclusion, he believed, accords with the view that antibacterial substances may operate by interfering with essential metabolites necessary for the growth of bacteria. Stamp,³ working on a similar hypothesis, found that extracts of streptococci contain a substance that antagonizes the action of sulfanilamide. Green⁴ noted that under certain conditions *Brucella abortus* is capable of releasing some factor into the culture medium that inhibits the action of sulfanilamide. He showed that the yield of the antisulfanilamide factor is greater when the *Br. abortus* is allowed to autolyze. He also demonstrated that this factor has a powerful growth-promoting effect, not only on *Br. abortus* but on other organisms as well.

Previously, McIntosh and Whitby⁵ and others had called attention to the fact that a particular concentration of sulfanilamide is not bactericidal to more than a certain number of bacteria, varying with the species. This observation was confirmed by Green, who noted, for example, that an inoculum of 2000 organisms in a 1:10,000 concentration of sulfanilamide showed, after a preliminary growth phase, progressive bacteriostasis and final

sterilization, whereas an inoculum of 3000 organisms finally grew out. This relation was precise and constant and could be accurately predicted. Green's observations all pointed to the conclusion that the antisulfanilamide factor responsible for overcoming the bacteriostatic effect is produced by the autolysis of dead and living cells. Finally, he pointed out a fact frequently overlooked—namely, that whereas it is generally considered that sulfanilamide is bacteriostatic to relatively few organisms, it tends to be forgotten that the sensitivity to it varies only in degree, though often very widely. Not one of many organisms tested by him was completely insensitive to 1:100 concentrations of sulfanilamide. He found, for example, that a small inoculum of the almost insensitive *Bacillus subtilis* was killed by a high concentration.

Finally, Woods⁶ found that yeast extracts contain a substance that, like those of Stamp and Green, reverses the inhibitory effect of sulfanilamide. The behavior and chemical properties of this substance suggested to him that it might be chemically related to sulfanilamide. Following this lead, he tested various substances having a chemical structure similar to that of sulfanilamide. One of these, *p*-aminobenzoic acid, was discovered to have a high antisulfanilamide activity. Woods found a constant relation between the concentration of sulfanilamide used and the concentration of *p*-aminobenzoic acid required to reverse its inhibitory effect. He believed that his findings provided strong confirmation of Lockwood's suggestion that the inhibitory effect of sulfanilamide on bacterial growth is based on an inactivation of bacterial enzymes, and that the inactivation is due to the competition for the enzyme between the metabolite essential for bacterial growth and the structurally similar sulfanilamide. Woods further suggested that the differences in sensitivity of different organisms to sulfanilamide inhibition are correlated with quantitative differences in ability to synthesize *p*-aminobenzoic acid.

The significance of the foregoing with respect to the prophylactic intraperitoneal application of sulfanilamide in gastrointestinal surgery will be clear when the following points are considered. Immediately after the construction of an anastomosis, whether done by an open or by a so-called "aseptic" technic, conditions exist that are most favorable for the effective action of sulfanilamide.

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The inoculum of bacteria along the suture line is small. If infection can be considered to exist at this time, it is presumably in a preinvasive stage and there is little or no protein digestion, and it may reasonably be assumed that antisulfonamide substances are not present in high concentration. By the local application of sulfanilamide along the suture line, an overwhelming concentration of the drug can be brought to bear on the small number of bacteria.

It has long been known that in the healing of anastomosed hollow viscera the first essential is the agglutination of the opposed serosal surfaces by a fibrin seal. In the absence of any gross technical error, secondary leakage of a suture line may occur as a result of bacterial action along it, causing interference with agglutination of the opposed serosal surfaces or lysis of the fibrin seal that has begun to form. If local bacteriostasis along the suture line can be maintained long enough to permit the formation of a firm fibrin seal, which requires only a few hours to take place, the danger of secondary leakage and peritonitis can be greatly diminished.

That the local implantation of sulfanilamide is effective in bringing about this result has been dramatically shown by Varco, Hay and Stevens.⁷ By this method they were able to reduce to zero the mortality from peritonitis in a series of complicated experimental gastrointestinal surgical procedures on 37 dogs—procedures that had hitherto carried a discouragingly high mortality from leakage at the suture line and subsequent peritonitis. They observed further that in the few dogs in the series that died of other causes, there was found at post mortem a firm fibrin seal between the opposed serosal surfaces, which contrasted sharply with the picture observed when dogs that had not been treated with sulfanilamide died of peritonitis in this interval, where there was little fibrin sealing and, hence, gross contamination from the stitch holes.

We have to date used sulfanilamide as a prophylactic agent by local implantation within the peritoneal cavity in 75 cases of gastrointestinal anastomosis or other operative procedures requiring the opening and closure of hollow viscera within the peritoneal cavity, excluding obstructive or Mikulicz resections. These cases are summarized in Table 1.

Sulfanilamide was used as the chemotherapeutic agent in all cases. The chemotherapy was limited to the intraperitoneal dose, with the single exception of a case of carcinoma of the sigmoid in which sulfaguanidine was given orally both preoperatively and postoperatively. We believe that this point is of major significance with respect to the incidence of toxic reactions. This has been

emphasized by Jackson and Coller,⁸ who observed no toxic reaction in a series of 33 cases in which sulfanilamide was given only intraperitoneally. In contrast with this, they report 9 cases of toxic hepatitis with jaundice in a series of 29 cases in

TABLE 1. Data on Cases.

OPERATIVE PROCEDURE	No of CASES	No of DEATHS
Gastric resections (1 transthoracic)	39	5
Taking down posterior gastroenterostomy, excision of gastroyejunocolic fistula and gastric resection	3	
Taking down posterior gastroenterostomy, excision of gastroyejunal ulcer	1	
Posterior gastroenterostomy	5	
Gastroduodenostomy	1	
First stage Whipple type of operation, posterior gastroenterostomy, cholecystojejunostomy and jejunoyejunostomy	1	
One stage duodenectomy; posterior gastroenterostomy, cholecystojejunostomy	1	
Right colectomy	6	1
Ileotransverse colostomy	4	
Resection of colon and rectosigmoid	7	
Sigmoidectomy and polypectomy	1	
Reduction of partial intussusception and excision of lipoma of colon	1	
Resection of ileum	3	
Taking down of end ileostomy, ileocecectomy	1	
Excision of ectocolic fistula	1	
Totals	75	6

which additional sulfanilamide was given. In our series, there was but one clear-cut toxic reaction, a toxic hepatitis occurring four days after a gastric resection. Complete recovery followed a stormy convalescence.

In the case in which sulfaguanidine was given preoperatively and postoperatively, mentioned above, a toxic hemolytic anemia was suspected on the second postoperative day, when the red-cell count and hemoglobin suddenly dropped from preoperative levels of 4,510,000 and 90 per cent, respectively, to 2,600,000 and 54 per cent. However, on the same day there was a discharge of dark blood from the wound, and subsequently large quantities of dark blood were passed rectally. We are inclined to believe that this represented a straightforward case of postoperative hemorrhage, rather than a reaction to the drug.

We are convinced that the danger of serious toxic reaction is slight when a single intraperitoneal dose of sulfanilamide is used, even when this dose is large.

The intraperitoneal doses of sulfanilamide employed in our series varied from 4 to 16 gm., with an average of 7.8 gm., and in 10 cases an additional amount (2 to 4 gm.) was left in the wound. When this study was first begun, we were influenced in favor of relatively large doses by the experience and recommendations of Thompson, Brabson and Walker⁹ in the intraperitoneal use of sulfanilamide in appendicitis. In the more recent cases, the usual intraperitoneal dose has been 6 to 8 gm.

Whereas sulfanilamide alone was used in all our cases, it seems likely that a mixture of sulfanilamide and sulfathiazole, as advocated by Key¹⁰ in orthopedic conditions, offers certain advantages. Throckmorton^{11, 12} has shown that in experimental animals some sulfathiazole remains visible within the peritoneal cavity for three to six days after implantation, whereas sulfanilamide remains visible for only six to twelve hours. The prolongation of the local effect that would be attained by the use of the more slowly absorbed sulfathiazole, its wider range of bacteriostatic activity and its more effective mobilization of cellular reaction all lead us to believe that a mixture of sulfathiazole and sulfanilamide may offer definite advantages.

In the series of 75 cases, there were 6 deaths, a mortality of 8 per cent. There were no deaths from peritonitis. Pulmonary embolism was the cause of death in 3 cases. In 2 of these, both gastric resections, the diagnosis was confirmed by autopsy. In the third case, a right colectomy, autopsy was not done, but the embolism occurred on the eighteenth postoperative day, when the patient was ready to be discharged.

In 2 of the remaining fatal cases, both gastric resections, the cause of death was pneumonia. In 1 of these cases, two of the silkworm-gut stay sutures gave way on the fifth postoperative day and dehiscence of the wound requiring resuture occurred, following which the patient developed pneumonia. Although death was clearly due to pneumonia, at autopsy an unsuspected pelvic abscess and an abscess in the right lumbar gutter were found, although all visceral suture lines were intact and there was no evidence of leakage. This patient had had a large polypoid carcinoma of the stomach that contained an intramural abscess with acute inflammatory changes in the adjacent tissues, which may, perhaps, have led to peritoneal contamination by organisms of unusually high virulence. Autopsy was not done on the second case, but clinically, death was due to pneumonia. The sixth fatality was in a trans-thoracic gastric resection, fifteen weeks after operation. An esophagogastric fistula with empyema and inanition was the cause of death.

Additional wound complications comprised minor infection in 3 cases, major wound infections in 2, transient pancreatic drainage after duodenectomy in 1, and transient duodenal fistula in 1. The last occurred in a case in which the duodenum was

divided a few millimeters above the papilla of Vater. There was one other wound dehiscence, after a right colectomy, apparently due to mechanical factors. An incarcerated loop of small intestine distant from the anastomosis perforated and resulted in a local peritonitis. This occurred, however, after the anastomosis had begun to function. This patient still has an ileal fistula but is recovering.

SUMMARY AND CONCLUSIONS

A series of 75 cases of gastrointestinal anastomosis, or some other operative procedure in which opening and primary closure of one or more hollow abdominal viscera were done, is reported in which sulfanilamide was applied intraperitoneally along the suture lines in the viscera. There were no deaths from peritonitis. Clear evidence of intraperitoneal infection was observed post mortem in only 1 fatal case, and in this case was not the cause of death. Only 1 patient had a toxic reaction to the drug, a toxic hepatitis with recovery.

Our experience with this series has convinced us of the value of the local intraperitoneal use of sulfanilamide along the suture lines after gastrointestinal anastomosis and in all cases with peritoneal soiling. We are satisfied that the danger of serious toxic reaction to the drug is slight if the intraperitoneal dosage does not exceed an average dose of 8 gm. in adults, and if this dose is not immediately preceded or followed by the additional administration of a sulfonamide.

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THE ANTI-THIAMINE FACTOR IN FISH

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EPIDEMICS of a severe and unusually fatal paralytic disturbance have been observed in animals when fish has been added to their diet.¹⁻¹⁰ A review of the circumstances of these epidemics of so-called "fish disease" and a study of the factor in fish responsible for them permit certain conclusions to be drawn concerning the use of fish in diets intended for human consumption.

FISH DISEASE IN ANIMALS

In 1936 Green¹ described a syndrome in foves that was induced by adding fresh fish to their diet. The clinical and pathological features of the disturbance resemble those of Wernicke's syndrome in man.¹¹⁻¹³ The first symptom is anorexia, which is usually followed in a few days by weakness, hyperesthesia, ataxia and death.¹⁻¹⁰ Post-mortem examination of the central nervous system reveals proliferation of the endothelium and adventitia of the small blood vessels, with varicose deformities and bilaterally symmetrical hemorrhages in the paraventricular nuclei and in the gray matter of the brain stem.¹¹⁻¹³ Studies of the cord and peripheral nerves are not reported, but degenerative lesions of the myocardium and fatty infiltrations of the liver have been described. Pups nursing from mothers affected with the disorder die early, without the histologic changes seen in the older animals.¹⁴

The disease is evidently one of thiamine deficiency, since it may be produced by thiamine deficiency under experimental conditions^{15,16} and may be cured by thiamine injections.^{1-6,8} The exact distribution of the factor in fish responsible for production of the deficiency has not been surveyed. The disease, however, has been observed following the consumption of carp, Atlantic Coast whiting, Pacific Coast mackerel, Lake Superior and Lake Michigan herring, suckers, smelts, mullets and great northern pike.^{7,8} Experiments with carp have demonstrated that the factor responsible is present in large quantity in the viscera and to a less extent in the heads, skin and scales. It does not seem to be present to a significant extent in the fish muscle. Thus, diets containing 20 per

cent of fish muscle were found to be innocuous, whereas diets containing 10 per cent of whole raw fish promptly produced symptoms.^{8,8}

Of critical importance, however, is not the amount of fish present in the diet, but rather the thiamine content of the diet as a whole and the length of time during which fresh raw fish is allowed to stand in contact with the thiamine-containing foods.^{15,16} Intimate mixing of the thiamine-containing constituents of the diet with portions of raw fish rich in the anti-thiamine factor is essential to production of the disease. Raw fish fed as a separate meal is harmless.⁶

CHARACTERISTICS OF THE ANTI-THIAMINE FACTOR

The anti-thiamine factor is destroyed by cooking,¹⁵ and also by drying in air at room temperature.¹⁶ The factor is of large molecular size and

TABLE 1. *Effect of pH on the Destruction of Thiamine by Carp Enzyme.*[§]

pH	THIAMINE DESTROYED %
6	40
7	60
8	90

§1 cc. of carp extract, 4 cc. of phosphate buffer and 25 microgram of thiamine, incubated for 30 minutes at room temperature

does not pass the membrane of living cells.^{16,17} It may be precipitated by protein precipitants and destroyed by peptic digestion.^{18,19} The reaction with thiamine appears to be enzymatic and to exhibit maxima at pH 9 and 60°C.¹⁸ Tables 1

TABLE 2. *Effect of Temperature on the Destruction of Thiamine by Carp Enzyme.*^{||}

TEMPERATURE (CENTIGRADE)	THIAMINE DESTROYED %
6°	30
29°	60
46°	100

||1 cc. of carp extract, 4 cc. of phosphate buffer (pH 7.0) and 25 microgram of thiamine, incubated for 30 minutes

and 2 illustrate the effect of pH and temperature on the rate at which the anti-thiamine factor of carp destroys thiamine.

CONCLUSIONS

From the foregoing review it appears that there is present in the viscera, heads, skins and scales

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of certain fish a proteinlike material capable of destroying thiamine in a manner suggestive of an enzymatic reaction. When portions of fish containing this anti-thiamine factor in significant quantity are allowed to come into intimate contact with the thiamine-containing constituents of the diet, the thiamine content of these foods may be lowered to a level no longer compatible with the maintenance of normal nutrition. Epidemics of thiamine deficiency explainable on this basis have been observed in animals to whose diet fresh raw fish has been added. Similar epidemics have not been observed in man.

There are a number of reasons why thiamine deficiency of this particular mechanism of origin may not be frequent in man. The portions of fish that are rich in anti-thiamine factor are for the most part those usually discarded in the preparation of fish for human consumption, that is, viscera, heads, skins and scales. Moreover, the destructive reaction with thiamine is definitely extrinsic since the factor itself is destroyed by peptic digestion. Because the factor is also destroyed by cooking or by drying, the only opportunity for its significantly affecting thiamine nutrition lies in those occasions where the major thiamine-containing constituents of the diet are mixed with whole raw fish and the mixture is allowed to stand at room temperature for some time before being cooked, eaten or dried. Under ordinary circumstances of diet preparation such circumstances are rare.

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MEDICAL PROGRESS

GENERAL ANESTHESIA

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THE present-day utilization of new anesthetic agents, modern gas machines, improved techniques and certain combinations of agents has given general anesthesia a flexibility and safety indicative of important progress in recent years.

The gas machine, the principal item in the anesthetist's armamentarium, not only enables him to administer anesthetic agents economically and conveniently but also aids in the maintenance of normal physiology, reduces the explosion hazard and provides an immediately available means of resuscitation. A modern gas machine used in conjunction with an endotracheal tube is practically indispensable for the application of positive intrapulmonary pressure in intrapleural surgery.

The following is a summary of the present status of the various agents used for general anesthesia.

INHALATION ANESTHESIA

Established Agents

Diethyl ether remains the standard drug for inhalation anesthesia, because of its wide margin of safety, relatively low toxicity, economy, and ease of administration, especially by the open drop method. Since the characteristic effects of ether are well known, their discussion in this article is unnecessary.

If considerable quantities of ether are used, a marked saving in cost may be achieved by bulk purchases. The *United States Pharmacopoeia* no longer states that ether is unsatisfactory for use twenty-four hours after the container is opened, and approves the use of 3-liter containers for storage. Ether is entirely satisfactory for clinical use for long periods after the seal of the container is broken,¹ and the use of 5-pound to 50-pound drums has been recommended. With proper precautions, ether may be drawn with perfect safety from the large containers into suitable small ones for operating-room use.

Cyclopropane is thought to be the most nearly ideal anesthetic agent, because of its potency,

rapidity of induction and recovery, apparent lack of toxicity, pleasantness to the patient and the high percentage of oxygen employed in administration. Whether it merits such a position is still debatable. When mixed with oxygen, it is highly explosive, and should be used only by one familiar with its toxic characteristics, since its action is rapid and the signs of degree of anesthetic depth are not so clear cut as those when ether is used.

The most commonly noted undesirable effects of cyclopropane are the various cardiac arrhythmias. They occur most frequently under deep anesthesia but also are observed under light anesthesia. Their control remains a problem, and whether they leave any long-lasting damage has not been determined. Arrhythmias may sometimes be inhibited by the simultaneous use of procaine² The protective action of the barbiturates has been confirmed³ and also denied.⁴ Morphine tends to exaggerate arrhythmias,^{2,3} and if large doses are used preoperatively, marked depression of respiration is likely to occur. The concomitant administration of cyclopropane and epinephrine is prone to produce ventricular fibrillation.

Since cyclopropane may have a tendency to act as a cardiac irritant, it probably should not be used in patients with cardiac impairment or with thyrotoxicosis. There have been reports of sudden deaths on the operating table of patients with thyrotoxicosis receiving this agent as an anesthetic. These deaths were probably due to ventricular fibrillation.⁵

Even in deep anesthesia troublesome laryngospasm occurs at times when high concentrations of cyclopropane are employed or when traction is exerted on the abdominal or pelvic organs.⁶

In most patients in whom a general anesthetic agent is indicated, with the exception of those undergoing abdominal surgery, cyclopropane produces satisfactory anesthesia. The degree of relaxation obtainable with safety is less than that obtained with ether; however, Guedel⁷ has offered a controlled-breathing technic to eliminate this difficulty.

As a supplemental agent for regional or spinal anesthesia, cyclopropane has proved valuable.⁸ In the presence of nausea, psychic disturbances or inadequacy of the principal agent, its use frequent-

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ly makes an otherwise unsatisfactory situation tolerable to both the surgeon and the patient. Cyclopropane has been used in obstetrics with good results.²

Ethylene is probably the most nontoxic of all inhalation agents with appreciable potency. Although explosive in anesthetic mixtures with oxygen, when properly used in patients with cardiac abnormalities it is safe and well tolerated. In many types of cases ethylene might well be employed with greater frequency. The concentrations required are comparable to those of nitrous oxide, but it is more potent than the latter, produces better relaxation and permits the use of somewhat higher percentages of oxygen.

Nitrous oxide is a relatively weak anesthetic gas. With an adequate percentage of oxygen, it is safe, but such a mixture frequently gives inadequate anesthesia, and consequently the flow of oxygen is reduced to a dangerous level. Sufficient morphine or a barbiturate given preoperatively often allows adequate anesthesia to be obtained with safe concentrations of nitrous oxide. Following the rectal administration of tribromethanol (Avertin) or Pentothal sodium, nitrous oxide is a most satisfactory anesthetic agent for many types of extra-abdominal operations. This combination is pleasing, especially to apprehensive patients or children, and is well tolerated by many poor-risk patients.

Ethyl chloride is a toxic drug with a narrow margin of safety.⁹ For general anesthesia it is dangerous because of its inherent tissue toxicity and because of its volatility, which may result in its vapor's rapidly displacing air in the air passages, with absorption of an overdose before the flow is controlled. A slow dropping on a gauze mask — not a spray — is the administration method of choice. Ethyl chloride should not be administered by one inexperienced in its use, but in the hands of a skilled anesthetist it is satisfactory for brief surgical procedures and as an induction agent preceding ether.

Chloroform is still considered too dangerous for frequent use. In addition to its toxicity to the liver and heart, it diminishes the plasma prothrombin,¹⁰ with consequent probable increase in bleeding hazards.

Divinyl ether (Vinethene) should not be considered a substitute for ether or cyclopropane. Because of its toxicity, it is contraindicated when hepatic or renal damage exists.¹¹ Because induction and recovery are rapid and because the drug is potent and causes little respiratory irritation, it has proved satisfactory for short surgical procedures requiring light anesthesia. Divinyl ether

is administered preferably by the open-drop method and is suitable for children, especially as an induction agent for diethyl ether. If divinyl ether is to be used for longer than thirty minutes, it should be volatilized with oxygen. This probably affords some protection against liver damage.¹²

New Agents

With the idea that new substances structurally resembling cyclopropane, ethylene and diethyl ether might be synthesized and proved to be valuable anesthetic drugs, a considerable number of chemicals have been developed. Some of them possess anesthetic qualities but because of toxicity or undesirable side effects are impractical for clinical use. However, *cyprome* and *cyclopropylmethyl ether* have been used with good results. *Cyprethylene ether*, first used in human subjects in November, 1941, is even more promising.¹³ It presents a high potency, produces marked relaxation, and can be administered in a mixture with high oxygen concentration.

For many years *trichlorethylene* has been known to possess anesthetic qualities. During the last eight or ten years a study of its characteristics and its effects on human beings has shown certain desirable qualities.¹⁴ Trichlorethylene has only a minor degree of toxicity for the liver and kidneys, produces little irritation of the respiratory passages, has slight effect on the body chemistry and decreases capillary oozing. In spite of these admirable qualities, trichlorethylene is used but little because vaporization is difficult, which makes it unreliable for third-stage anesthesia, and because in many cases inadequate muscular relaxation results.

Although trichlorethylene is usually considered to be noninflammable,¹⁵ recent work has shown that, whereas this is true for mixtures of air and trichlorethylene under ordinary conditions of temperature and pressure, it is probably not true of mixtures of this drug with pure oxygen. Recently published figures indicate that mixtures of trichlorethylene and oxygen are inflammable within the limits of 10.3 per cent to 64.5 per cent trichlorethylene.¹⁶

It has recently been shown that this drug is capable of producing cardiac arrhythmias,¹⁷ an undesirable feature in anesthesia.

Tetrachlorethylene, a nonexplosive, noninflammable liquid with anesthetic properties, is probably nontoxic.¹⁸ In man a moderate degree of surgical anesthesia can be produced, but its disadvantages probably make it of little value clinically. Tetrachlorethylene is difficult to volatilize and is irritating to the mucous membranes and the skin.¹⁹

EXPLOSION HAZARDS

Although anesthetic mixtures in oxygen of ether, cyclopropane and ethylene are explosive, they are safe when proper precautions are taken to prevent static sparks and to exclude cautery or sparking electric apparatus from the vicinity. Modern operating rooms in which switches and wall plugs are designed to minimize the possibility of igniting inflammable mixtures, and in which good ventilation is provided, together with the use of an inter coupler and a tightly closed breathing system have done much to eliminate the explosion hazard. The likelihood that a spark or flame will ignite a mixture decreases markedly when its distance from the leaking mixture is two feet or more.

Efforts have been made to find a suitable combination of an anesthetic agent, oxygen and an inert gas—for example, helium—that is non explosive. Several such combinations have been devised.¹⁹ Their practical value is doubtful, however, because not much variation in the relative proportions of their constituents is possible. Present day gas machines are not considered accurate enough to allow their use with any degree of safety.

RECTAL ANESTHESIA

The most widely used drug for rectal anesthesia is *tribromoethanol* (Avertin) in *amylene hydrate*. It was originally intended for use unsupplemented, but since the doses required proved too depressing, it is now employed as a basal anesthetic. In combination with nitrous oxide, it furnishes excellent anesthesia in thyroid surgery.²⁰ In apprehensive patients and children, its use does much to allay preoperative fear and facilitates rapid, smooth induction of anesthesia.

This drug might be more widely used for basal anesthesia except that it often produces a prolonged period of postoperative respiratory depression, tending to allow secretions to accumulate in the respiratory passages. This lengthy period of postoperative unconsciousness necessitates more intensive nursing care.

Pentothal Sodium, although primarily intended for intravenous anesthesia, has proved an effective and safe basal anesthetic when given rectally and followed by nitrous oxide or a small amount of cyclopropane.²¹ The action of the drug when administered rectally is essentially the same as that when given by the conventional intravenous route. Rectal installation should take place half to one hour previous to beginning the inhalation phase of the anesthesia. In healthy adults the dose is 1 cc of a 10 per cent solution for every five pounds of body weight. A smaller dose is used when indicated by the patient's age or condition.²¹ In infants, *Pentothal Sodium* has been used in this manner in

doses of 0.8 cc of a 2.5 per cent solution per pound of body weight.²²

Lyval Soluble is also a satisfactory basal anesthetic when given rectally one hour preceding the inhalation anesthetic in doses of 0.2 cc of a 10 per cent solution per pound of body weight.²³

INTRAVENOUS ANESTHESIA

Clinically intravenous anesthesia is today achieved almost solely by the use of *Pentothal Sodium* or *Evipal Soluble*, the two outstanding short acting barbiturates. The former drug is given the preference by most anesthetists in their routine work, since the rapidity of induction and the infrequency of postoperative nausea and vomiting make it most acceptable to patients.

When *Pentothal Sodium* is the sole anesthetic agent, the surgical procedure is limited generally to forty five minutes and does not require a considerable degree of muscular relaxation. A wide variety of difficult types of surgery, including intra abdominal procedures, have been performed successfully under *Pentothal Sodium* alone, but when one considers the danger to the patient of the required deep anesthesia and the technical difficulties that the surgeon is likely to encounter in its frequent use, it seems best in such cases to rely on other agents commonly available in civilian practice.

In military surgery, however, especially under front line conditions, *Pentothal Sodium* is an extremely valuable and widely used drug. One surgeon²⁴ in describing his experience in treating battle casualties said that the wounded men were brought in frightened, heavily narcotized, tired and in more or less shock. The necessary surgical procedures usually required not over an hour, and in about 95 per cent of the cases intravenous anesthesia was employed. In the Dieppe raid, *Pentothal Sodium* was used as the sole anesthetic agent in treating 51 per cent of the casualties.²⁵ The usual rapid recovery from the anesthetic agent with few aftereffects allowed rapid evacuation of the patients to hospitals some distance from the front. Since *Pentothal Sodium* is noninflammable and easily transported, prepared and administered, it is highly acceptable under these conditions.

The scope of intravenous anesthesia has been greatly widened by its use in combination with other methods. As a supplement to spinal anesthesia, it eliminates the nausea, retching and painful traction stimuli often accompanying abdominal procedures, and does not cause the increased diaphragmatic excursions often noted when an inhalation anesthetic agent is used as a supplement.⁸ Electric apparatus and cautery may be employed freely when a spinal anesthetic and *Pentothal Sodium* are used.

Combined with local infiltration, regional or splanchnic block or nitrous oxide, Pentothal Sodium produces good anesthesia, especially for poor-risk patients.²⁶ Diabetic patients also tolerate the drug very well.²⁶ Certain hazards accompany its use, and the anesthetist should be prepared with means for combating them. Respiratory failure may result from an overdose or from laryngospasm. The latter is especially prone to occur in the presence of excessive amounts of mucus or blood or when instrumentation in the pharynx is performed. Laryngospasm may be prevented if the pharynx and glottis are sprayed with a 10 per cent solution of cocaine immediately prior to the injection of the Pentothal Sodium. Hiccups occurring under the drug usually cease if intravenous atropine (1/75 gr. in adults) or cyclopropane is administered. Atropine should be given routinely before intravenous Pentothal Sodium, and a preoperative sedative such as morphine allows the use of smaller doses.²⁷ The continuous administration of 100 per cent oxygen during the anesthesia has been recommended. On the basis of animal experiments, Beecher and Moyer²⁸ have questioned the wisdom of giving 100 per cent oxygen to patients with respiratory depression under Pentothal Sodium anesthesia; ordinarily a low concentration of oxygen in the blood stimulates the respiratory center when the sensitivity to carbon dioxide is diminished, and the use of 100 per cent oxygen removes this stimulus. The use of Pentothal Sodium anesthesia is also considered unwise when hepatic, renal or serious cardiac disease exists, or when any condition that may interfere with adequate pulmonary ventilation is present.²⁷

Although the subject is controversial, some reports indicate that the barbiturates tend to prevent or retard the onset of shock.^{26, 29}

Clinically, there is ample evidence that Pentothal Sodium is not contraindicated when the patient has been receiving sulfonamide therapy.²⁷

Pentothal Sodium may also be used as an induction agent prior to the administration of the principal agent and, if desired, can be given in the patient's room. This drug is valuable as an anti-convulsant.

Pentothal Sodium may be prepared in bulk solution. Five grams of the drug in 200 cc. of sterile distilled water gives a 2.5 per cent solution, which is satisfactory for use for several days or as long as the solution remains clear. This concentration is the one most widely used at present, since better control of the dosage is obtained, since accidental extravenous injection is less likely to produce undesirable tissue damage and since the incidence of phlebitis is decreased.

Recently published data show that the use of

paraldehyde as an intravenous anesthetic agent has probably been responsible for a number of deaths.³⁰ Animal experiments confirmed the fact that paraldehyde was no doubt the cause of the post-mortem findings in these cases. With this in mind, paraldehyde should not be used for intravenous anesthesia, especially since Pentothal Sodium is safe and is readily available in most hospitals.

PREMEDICATION

Morphine, the *barbiturates* and the *belladonna derivatives*, atropine and scopolamine, continue to maintain their status as the standard drugs for preoperative medication. Morphine may be administered intravenously a few minutes before the induction of anesthesia, if the usual subcutaneous dose was omitted or proved insufficient to produce the desired sedation in a reasonable length of time.³¹ Morphine by the intravenous route should be given slowly, preferably in smaller doses than when given subcutaneously, and administration should be stopped if dizziness, numbness, tingling or other untoward reactions occur.³¹

A new synthetic drug, *1-methyl 4-phenyl-piperidine 4-carboxylic acid ethyl ester hydrochloride* (Demerol), has made its appearance as a substitute for morphine, especially if the supply of the latter should be threatened because of wartime conditions. It is one of a series of piperidine compounds, resembles atropine structurally, and possesses some of the properties of the latter, in addition to being a satisfactory analgesic and sedative. Demerol is said to be comparable to morphine and to be as reliable as the latter in the recommended dosage. The atropine-like properties of the drug are its ability to cause drying of the mucous membranes and its spasmolytic effect. Since it does not depress the cough reflex as does morphine and is effective for pain originating in serous membranes and smooth muscle, it may prove to be valuable in postoperative treatment. Whether its continued use will result in habituation has not been determined.^{32,33}

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 29361

PRESENTATION OF CASE

First admission. A thirty-five-year-old volunteer war worker entered the hospital because of paresthesias of the fingers of nine weeks' duration.

For the previous nine weeks he had noticed tingling of the fingers; he had become noticeably weak, especially in the arms. His physician found the hemoglobin to be 65 per cent and gave him iron and cod-liver oil without any benefit. During the week before entry the tongue felt thick.

At the age of twenty-two he began to lose weight; he was told that his systolic blood pressure was 200 and that "he was threatened with tuberculosis." He went south, "took it easy" for four years and had worked hard ever since. The hypertension apparently disappeared. About a year before entry he was turned down by the draft-board physician for a cardiovascular defect, but was not told what it was.

Physical examination on admission showed a well-developed, well-nourished man. There was slight diminution to light touch and pinprick around the mouth. The tongue was slightly tremulous but not atrophic. The upper extremities were normal in color and ability to sweat. The strength of all muscle groups was definitely weakened, most conspicuously in the shoulder girdles—he could barely raise his arms above his head. There was no muscular fibrillation. He could not stand or walk on his toes or heels, or rise from a squatting position. The abdominal and back muscles were relatively strong. The Romberg sign was positive. There was no muscle tenderness, but straight leg-raising carried to 45° caused pain bilaterally. There was sensory loss for touch and pain in the distal portions of the arms and legs. Vibratory sense was diminished over the wrist, and lost over the malleoli. The triceps reflexes were barely present; the biceps, radial, ankle and knee jerks were absent; abdominal and cremasteric reflexes were present. The heart, lungs and abdomen were normal.

*On leave of absence.

The blood pressure was 134 systolic, 106 diastolic. The temperature and respirations were normal; the pulse was 84.

The white-cell count was 8700, with 66 per cent neutrophils, and the hemoglobin 14.5 gm. The urine was normal. A gastric analysis was normal. A blood Hinton test was negative. A lumbar puncture gave an initial pressure of 150 mm. (water). There were no cells in the spinal fluid; the total protein was 133 mg. per 100 cc., and the gold-sol curve 0011222200. A spinal-fluid Wassermann test was negative.

X-ray examination of the chest revealed no definite increase in the size of the heart. The apex of the heart was somewhat rounded, and the aorta was slightly tortuous; the lungs and the diaphragm were normal.

The patient was discharged, unimproved, after five days.

Final admission (two weeks later). The patient returned because of difficulty in breathing. After his discharge there was gradual progression of weakness. On one occasion he fell and had difficulty getting back to bed. For two days prior to admission there was some difficulty in breathing, and slight difficulty in swallowing and talking. There was no increase in sensory symptoms.

The weakness had increased, and it involved not only the arms and legs but also the abdomen, back and neck and intercostal muscles. Chest expansion was limited to 3 cm. at the level of the nipples. The voice was husky and frequently trailed off into a whisper. The facial, ocular and masseter muscles seemed to be normal. All the tendon reflexes, as well as the abdominal and plantar reflexes, were absent.

The blood pressure was 140 systolic, 100 diastolic. The temperature was 98.6°F., the pulse 90, and the respirations 20.

The patient was given hot packs (Kenny therapy). He developed cramps of the flexors of fingers of both hands, which recurred during his entire stay. On the third day he had so much respiratory difficulty that he had to be put into a respirator. Following this episode he was able to elevate his arms overhead and to raise his legs from the bed, but his fingers and toes remained very weak. There was preservation of the sensations of light touch and pinprick throughout. Profound disturbance of the vibration and position senses was noted in all extremities. There was minimal tenderness of the calf muscle. A lumbar puncture gave an initial pressure of 100 mm. (water), and the spinal fluid contained no cells; the total protein was 190 mg. per 100 cc.

During the next two weeks, treatment with hot packs was carried out. On the whole there was

no improvement or any definite progression. One observer stated that there was slight bilateral facial weakness. Toward the end of this period, however, the respirations became increasingly shallow, rapid and labored. Examination at that time revealed more tenderness and perhaps more weakness. Sinus arrhythmia, with a rate of 104, developed. The blood pressure was 150 systolic, 115 diastolic. Examination of the lungs was unsatisfactory, but they seemed to be clear.

On the twentieth hospital day the patient became weaker and was unable to raise secretions or to swallow, or to breathe outside the respirator. He died on the twenty-first hospital day.

DIFFERENTIAL DIAGNOSIS

DR. AUGUSTUS ROSE: I assume that discharge from the hospital at the time of the first admission was not because the attending physician believed that the patient was over his illness. There undoubtedly were other reasons, economic or something of that nature. There is no mention of mental symptoms, so I shall assume that the patient was normal mentally.

This case offers little or no difficulty in diagnosis, yet it raises the important question of polyneuritis and a discussion of the pathology of the condition. Ignoring the details of the history, this is the case of a thirty-five-year-old man who, after nine week of paresthesia and weakness of the extremities, developed cranial-nerve palsies and died in respiratory paralysis. The spinal fluid showed a high total protein without cells. This is the clinical picture, but fortunately is not the usual outcome of the condition known as infectious polyneuritis. It also goes under a number of other names: infective neuronitis, radiculoneuritis, polyneuritis with facial diplegia, Guillain-Barré syndrome and so forth.

Polyneuritis is a clinical picture, the essential feature of which is impairment of function of many peripheral nerves, resulting in a more or less symmetrical distribution of muscular weakness and sensory loss. This general picture is usually present in all cases regardless of the etiology of the neuritis. In many cases, however, there are characteristic clinical differences between the various types of polyneuritis. In most types of peripheral neuritis the weakness and sensory loss are chiefly confined to the distal portions of the extremities. In infectious polyneuritis, as illustrated by this case, muscular weakness also involves the proximal muscles of the extremities and the muscles of the trunk. In addition, muscles innervated by the cranial nerves arising from the pons and medulla are often partially or completely paralyzed.

The etiology of polyneuritis remains somewhat confused. In recent years we have heard more

and more about vitamin deficiency, with evidence accumulating to show that a number of different factors contribute to the clinical picture. The role of vitamin deficiency is seen to contribute to the neuritis associated with diabetes, pregnancy and certain other metabolic and toxic conditions. It has been stated to be due to a virus, transferable to monkeys, but this has not been verified. Clinical evidence, however, supports the idea of an infectious agent. Characteristically the syndrome so well described in this case comes on a few days following a mild systemic infection in which there is a mild elevation in temperature, coryza and general malaise. Frequently also, the onset of neuritic symptoms is accompanied by slight fever. The absence of these symptoms in this case, however, does not alter the probable diagnosis, for the systemic infection may be so mild that it is overlooked or forgotten by the time the more dramatic paralytic symptoms develop. The spread of symptoms is usually fairly rapid and, not infrequently, may ascend from the lower extremities, reaching the neck and bulbar-supplied muscles last. This type of spread has led some observers to infer that the disease is located in the spinal cord as well as in the peripheral nerves. In such cases the old question of Landry's ascending paralysis is considered in the differential diagnosis, although that is only a name applied to a train of symptoms and is not a disease entity. In 1927, Dr. Viets¹ published a series of cases from this hospital in which he stressed the frequency of bilateral facial weakness without evidence of involvement of other cranial nerves. In the cases of this group coming to autopsy, pathologic changes were found in the motor cells of the spinal cord and brain stem.

Great emphasis should be placed on the spinal-fluid findings in infectious polyneuritis. The high total protein, which is almost always present in varying degree, is not accompanied by an increase in the cells. This dissociation was emphasized by Guillain, Barré and Strohl² and has come to be almost pathognomonic.

Returning to this particular case, I see no reason for believing that the low hemoglobin or the signs of cardiovascular disease played any role in the patient's final illness. He certainly had a mild degree of hypertension—as shown by a persistently elevated diastolic pressure and by rounding of the cardiac apex by x-ray. There are no leads suggesting disease other than that within the nervous system, or any specific etiologic agent, such as arsenic or alcohol.

It is not safe for one to put all his eggs in one basket. Yet I am at a loss to suggest any diagnosis other than infectious polyneuritis. I shall be interested in hearing a discussion of the pathology of the case by Dr. Kubik. He has often told us

that the pathology is confined to the peripheral nerves and characterized by round-cell infiltration.

DR. JAMES B. AYER: This patient was under my observation for the greater part of his illness. The diagnosis was made on the first admission, at which time he was discharged slightly improved, apparently just from rest in bed. Later he developed respiratory difficulty and was sent back to be near a respirator.

I question whether there was a sensory disturbance of the face. Sensory disturbance in the cranial nerves in this disease are extremely rare. I was never convinced that he had facial paralysis, and only once did anyone think he had it; I repeatedly looked for it because it is so characteristic.

There was no evidence of cerebral involvement. The patient was always intelligent, and there was nothing that suggested encephalitis. Regarding the Kenny treatment, both legs and arms were more comfortable when packed; even respiration was benefited, and one could get about 1 cm. greater respiratory excursion after the Kenny pack had been applied to his chest. He thought it was better than the respirator, which was surprising to me, and I suggest this as an agent to be used in such cases.

We could never make any diagnosis other than what Dr. Rose has made.

DR. HENRY R. VIETS: I saw this man during the last week of his illness. On at least one occasion I thought he had lower facial paralysis, but it was partial and certainly not marked.

It seems to me there is no question about the diagnosis. The most difficult point in regard to polyneuritis from the clinical point of view is the prognosis. This man was a young, husky individual, and all during the course of his illness both Dr. Ayer and I were doubtful about the prognosis, even believing at times that he might recover. Certainly we have had patients as sick as he was up to the last day of his illness who have made a total recovery. One of the surprising things is that they do recover so well and recover so completely in view of the seriousness of their illness. The fact that, in this case, the shoulders were severely involved almost from the start made me a little cautious about the prognosis because the lesion was getting close to the fourth cervical segment, where the phrenic nerve comes off. We should have taken more into consideration that he was close to the danger line at all times.

CLINICAL DIAGNOSIS

Infectious polyneuritis.

DR. ROSE'S DIAGNOSIS

Infectious polyneuritis.

ANATOMICAL DIAGNOSIS

Infectious polyneuritis.

PATHOLOGICAL DISCUSSION

DR. CHARLES S. KUBIK: There have been 5 or 6 deaths from infectious polyneuritis in this hospital, with autopsies in 3 of them. In the other 2 autopsied cases, death occurred on about the tenth day of the illness. This one was unusual. The steady progression of symptoms continued for approximately fifteen weeks and eventually resulted in death. The pathological findings have been essentially the same in all three cases.

The outstanding feature is an infiltration of spinal nerve roots, spinal ganglions and peripheral nerves with lymphocytes (Fig. 1). Special stains show degenerative changes in the myelin sheaths

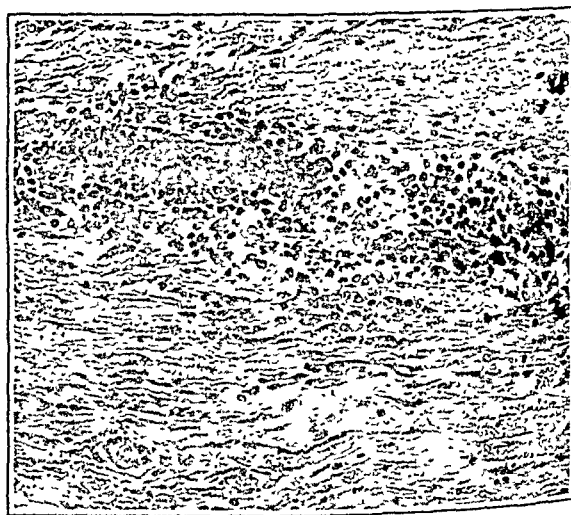


FIGURE 1. *Lymphocytic Infiltration of Peripheral Nerve.*

and axis cylinders, but only rarely complete destruction of fibers. Except for an axonal reaction in the anterior-horn cells, secondary to the degenerative changes in the nerve roots and nerves, nothing abnormal is found in the spinal cord, brain stem or brain.

DR. ROSE: So the disease is not entirely peripheral in an anatomic sense.

DR. KUBIK: I should consider the nerve roots as part of the peripheral system. In any case, there is no cellular infiltration in the brain or cord.

We have found pathologic changes in all cases, although it is sometimes said that there are no distinctive lesions. Since they were found in only a few out of many sections of peripheral nerve in this case, it is easy to understand why these lesions

may be missed. I should suspect that the negative findings are based on cases of deficiency neuritis that were mistaken for cases of infectious polyneuritis. Although the two conditions may resemble each other clinically, they probably have nothing in common so far as etiology is concerned. I might add that there is no cellular infiltration of the nerves in deficiency neuritis. As Dr. Rose has said, there is no good proof that infectious polyneuritis is really an infection. Bradford, Bashford and Wilson³ thought that they had transmitted the disease to monkeys, but their claims have not been confirmed. Material from 2 of our cases was inoculated into the brains of monkeys with negative results.

DR. ROSE: Has there been, to your knowledge, any case in this hospital in which there were cerebral symptoms?

DR. KUBIK: I do not know of any.

DR. ROSE: Do you remember any, Dr. Ayer?

DR. AYER: No.

DR. ROSE: Some textbooks speak of mental disturbances—not unlike those seen in Korsakoff's psychosis.

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CASE 29362

PRESENTATION OF CASE

A thirty-one year old housewife was admitted because of jaundice of six days' duration.

Nine days before admission she developed soft, mushy, yellow, loose stools, which persisted for three or four days. Six days before entry she noticed jaundice of the skin, which became progressively deeper. Three days later she was seized with a sharp pain in the neck, both shoulders and both arms down to the elbows. The attacks lasted for fifteen minutes and left her completely exhausted. She had two similar attacks in the following two days.

She had had arthritis and rheumatic pneumonia at the age of twenty-one and "milk leg" at the age of twenty-seven. Two years prior to admission she developed Raynaud's disease, for which she had three hospital admissions over a period of one year. Bilateral dorsal and lumbar sympathectomies were performed with considerable relief. For the previous two years she had suffered from recurrent, slowly healing ulcers of the lower legs.

Physical examination showed a markedly jaundiced woman. The lungs were clear. There was a short systolic and a mid-diastolic murmur in the aortic area, transmitted to the neck. The extremities were warm and dry. There were many healed scars, with turgor and diminished subcutaneous tissue, on both hands.

The temperature was 99°F, the pulse 80, and the respirations 20.

Examination of the blood revealed a red-cell count of 3,690,000, with a hemoglobin of 10.5 gm, and a white cell count of 12,600, with 57 per cent neutrophils. The urine had a specific gravity of 1.009, with a + test for bile and a negative test for urobilinogen; the sediment contained 4 or 5 white cells per high power field, a culture showed many colonies of colon bacilli. The stools were guaiac negative. The blood nonprotein nitrogen was 18 mg per 100 cc, and the van den Bergh 8.2 mg direct, 12.3 mg indirect. The protein was 7.6 gm per 100 cc, the albumin being 3 gm, and the globulin 4.6 gm—an albumin globulin ratio of 0.7. A blood Hinton test was negative. The blood phosphorus was 2.1 mg per 100 cc, and the phosphatase 7.9 Bodinsky units. The cephalin flocculation test was ++++ in twenty-four and forty-eight hours.

The jaundice seemed to increase. On the sixth hospital day the patient had a mild chill and a slow rise of temperature to 104.5°F about one and a half hours later, after which it fell slowly to 101.5. She became incontinent, disoriented, drowsy and restless. The breath was 'mousy'. There were edema and ascites. The white cell count on the seventh hospital day was 11,400. The urine gave a ++ test for albumin and a + test for bile; it contained innumerable white cells. The patient was given daily transfusions, intravenous 25 per cent glucose and a high vitamin and high carbohydrate diet. One blood culture was reported positive for colon bacilli in both flasks. A blood culture taken on the next day was sterile. Giemsa stains of a blood smear failed to show any leptospira and guinea pigs inoculated intraperitoneally with the patient's blood remained well.

On the ninth hospital day she became stuporous. The nonprotein nitrogen was 22 mg per 100 cc, and the protein 8.6 gm. The white cell count was 22,250. On the tenth hospital day, the temperature rose to 104.5°F and the patient developed labored jerky respirations with many pauses and died.

DIFFERENTIAL DIAGNOSIS

DR. ALSTON M. BRUES: This case, I think, can be described as icterus gravis or malignant jaundice.

In other words the patient had fulminating hepatic failure. This state is typified by acute yellow atrophy but may be simulated by other processes causing rapid destruction of liver tissue, notably suppurative processes. Acute yellow atrophy generally runs a course of about two weeks. It begins with mild intestinal symptoms and perhaps some fever and is thought to be catarrhal jaundice. There may be vomiting. It is interesting that this patient, so far as the record goes, did not suffer from vomiting throughout her illness. I should expect it to have occurred, and I am unable to account for its absence.

After several days in the hospital the picture suddenly became critical. This phase was ushered in by nervous symptoms, and it has been recognized for at least seventy-five years that the dividing line between benign and fatal jaundice—between catarrhal jaundice and acute yellow atrophy—is drawn by nervous or mental symptoms. These symptoms indicate "cholemia," in other words, hepatic failure. One generally sees in fulminating hepatic failure something that was not present in this patient, namely, a bleeding tendency due to a fall in the prothrombin content of the blood.

The mousy odor to the patient's breath is a subjective observation indicating that hepatic failure was being considered and that the observer thought that he had evidence for it. The patient late in the course of the disease had intermittent fever, as is seen late in hepatic failure.

Concerning the laboratory findings, the maximal cephalin flocculation test gives evidence of hepatic-cell failure. There was a very slight rise in the blood nonprotein nitrogen, which in itself is of no importance. If, when broken down, it showed a rise in the amino nitrogen and a marked fall in urea, that would be evidence of "cholemia." The plasma showed only a moderate increase in globulin, and a moderate decrease in albumin. This indicates that the process was of relatively short duration—in other words, that it did not supervene after a long course of mild hepatic failure or cirrhosis. This finding, which was made on admission, is commonly seen even in cases of simple catarrhal jaundice.

We ought to consider whether the jaundice was obstructive. I find no mention of the stools except for the observation before the onset of jaundice, when they were said to be light yellow. The phosphatase in true obstructive jaundice with relatively normal hepatic-cell function should be somewhat higher than it was here; I would expect it to go up to 10 or more units. The absence of urobilinogen suggests obstruction,—that is, failure of bile to reach the intestines, where urobilinogen is formed,—but it is well known that in

acute hepatitis the urobilinogen may be absent during the acute stage and recovery heralded its reappearance. Whether this is due to functional obstruction or to loss of function of hepatic cells, I do not know, but I shall take the absence of urobilinogen to indicate only that the patient did not have hemolytic jaundice.

There is one secondary diagnosis that I should like to discuss at some length—a suppurative cholangitis presumably secondary to biliary obstruction. We recall that, particularly after the onset of the patient's illness, there was pain. This pain was suggestive of gallstone colic in its sudden exhausting character. The distribution in the shoulders and the neck is not entirely characteristic of gallstone colic but is consistent with biliary calculus. Had that pain been not quite severe it would be easy to say that it was due to an initial swelling of the liver in the early stage of acute hepatitis. The second fact favoring cholangitis is colon-bacillus bacteremia observed on one occasion. This suggests that there was infection, perhaps of the biliary tract, with this organism. However, it is well known that such bacteremia may occur in the later stages of a debilitating illness, and it has indeed been mentioned as a common finding in acute yellow atrophy. Against cholangitis is the fact that fever is a prominent feature of this picture only in its late stage; the patient does not have a septic fever during the first three quarters of the illness. The differential count also shows that the neutrophils were relatively low, implying lymphocytosis. This is characteristically seen in catarrhal jaundice, and is not characteristic of a septic process.

It is obvious that Weil's disease was considered and presumably ruled out by the inability to produce disease in guinea pigs; agglutination tests with the patient's serum were not performed. In Weil's disease, as in yellow fever, we should expect more renal damage than this patient exhibited.

Another infectious process that might be considered is endocarditis, especially since the patient was thought to have rheumatic heart disease. It is improbable that endocarditis produced so much damage in the liver with no apparent damage elsewhere. Pylephlebitis entails the same objection as suppurative cholangitis, namely, that the patient was not septic during the greater part of her illness.

If we consider acute yellow atrophy the best diagnosis, we obviously ought to consider the known etiologic factors, such as the toxic effect on the liver of specific poisons. Since she was a housewife, presumably she did not work in a triethylol factory or was not exposed to other industrial hazards. There is no evidence for any other

specific poison, such as chloroform or phosphorus, that might have caused atrophy of the liver. The incidence of acute yellow atrophy is high in pregnancy; nothing in the record suggests that the patient was pregnant, but there is no definite evidence to rule it out. It has been suggested, on purely theoretical grounds, that acute yellow atrophy may be due to the regurgitation of proteolytic pancreatic juice up the bile duct; however, unless the pathologist discovered a stone in the ampulla, I hesitate to make any such diagnosis.

Before I utter a final diagnosis I should like to ask if any competent observer noted that the liver was enlarged during the terminal two or three days.

DR. WILLIAM BECKMAN: At first, it was thought to be. Toward the end no one was able to feel it.

DR. BRUES: My final diagnosis is acute yellow atrophy of the liver, to which I shall add rheumatic heart disease and probably mild aortic stenosis and regurgitation.

DR. CASTLEMAN: One thing not brought out in the record is that the patient pursued a very benign course during the first five days in the hospital. We thought she had catarrhal jaundice, but we were puzzled by the fact that she had no nausea or vomiting. On the fifth day she had a violent, shaking chill, and the blood culture taken at that time was the one that was positive for colon bacilli; subsequent cultures were negative. From that day on, she went downhill and was febrile.

CLINICAL DIAGNOSES

Acute hepatitis.
Septicemia (colon bacillus).

DR. BRUES'S DIAGNOSES

Acute yellow atrophy of liver.
Rheumatic heart disease (? aortic stenosis and regurgitation).

ANATOMICAL DIAGNOSES

Subacute yellow atrophy.
Acute pycelonephritis.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy showed a liver that weighed about 970 gm.; the normal liver in a woman of this age and size weighs about 1500 gm. The liver was mottled yellowish purple, with slightly yellowish-green areas of apparent regeneration. Microscopic examination confirmed the marked atrophy and areas of regeneration. The atrophic regions contained an occasional single liver cell and a few remaining bile ducts. There was a fair amount of regeneration, but very little fibrosis. The process had probably been going on at least three weeks and therefore might perhaps be called subacute yellow atrophy.

The heart was small and perfectly normal. Both kidneys were enlarged and swollen and contained numerous small abscesses, which accounted for the colon-bacillus septicemia and certainly must have been an added burden to a patient with severe liver insufficiency. The biliary tract was normal; there were no stones or dilation of the bile ducts.

DR. WILLIAM B. BREED: What was the sequence in this case? Did the kidney infection and the septicemia precipitate the liver disease? What was the etiology of the acute yellow atrophy?

DR. CASTLEMAN: I cannot explain the sequence in this case. It is believed that catarrhal jaundice and acute yellow atrophy may have the same etiology. Thus, if the patient with jaundice, due perhaps to some infection, gets well it is called catarrhal jaundice; if the patient dies, it is called acute yellow atrophy. Several years ago during an epidemic of catarrhal jaundice in Sweden, the incidence of acute yellow atrophy was also increased.* Most of the cases of acute yellow atrophy that we have seen have been due to drugs, such as arsenamine and cinchophen-containing products.

*Bergstrand, H. *Über die akute und chronische gelbe Leberatrophie mit besonderer Berücksichtigung ihrer epidemischen Auftretens in Schweden im Jahre 1927.* 114 pp. Leipzig: Georg Thieme, 1930.

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If we consider acute yellow atrophy the best diagnosis, we obviously ought to consider the known etiologic factors, such as the toxic effects on the liver of specific poisons. Since she was a housewife, presumably she did not work in a trinitrotoluol factory or was not exposed to other industrial hazards. There is no evidence for any other

ceeding 650,000 for the first time since 1928. More over, the proportion of stillbirths to total births declined in the third quarter of the year to the lowest level on record, and the infant mortality approached the record low level of 50 per 1000 live births established in 1939.

These figures are not compatible with nationwide malnutrition, nor would they be found in a nation facing defeat after more than two years of war. They reflect rather, as the bulletin phrases it, the inspiring resilience of England's people under stress.

In general, despite wartime conditions and air raid casualties, the death rate in England last year was restored to its prewar level. Epidemic meningitis, always a war disease, markedly increased after the outbreak of hostilities, in 1942 its morbidity fell to about half that of 1940-1941, with, of course, under modern methods of treatment, an extremely low mortality rate. Tuberculosis, which had increased sharply in 1940 and 1941, showed a much lower incidence, the improvement being most noticeable among women and children. Deaths from diarrhea and enteritis among infants and young children increased slightly over the rate prevailing in 1941, but the deaths from diphtheria fell off sharply and epidemic respiratory diseases were conspicuous by their absence. Deaths from diabetes dropped,—overeating has not been an outstanding fault in England in the last three years,—and the mortality from peptic ulcer showed a sharp decline, furnishing as fine a bit of evidence as could be found that the emotional stress of recent years has been relieved. The suicide rate was lower, further illustrating the fact that men rarely despair of life when they have a job in hand, and the air raid deaths continued their decline from the dreadful month of September, 1940, when nearly 7000 civilians were killed. Even fatal road accidents, which have been a black mark on the escutcheon, declined 24 per cent last year from the peak of 1941.

These conditions may not continue, and the middle two of the famous horsemen may again ride with their flanking companions, but at least

for the present, it can be said that a superb job of adjustment to war conditions has been done and that thumbs are still up in Merry England.

MEDICAL EPONYM

CUSHING'S DISEASE

Dr Harvey Cushing (1869-1939), professor of surgery at Harvard Medical School, first described this disease in a paper entitled "The Basophil Adenomas of the Pituitary Body and Their Clinical Manifestations (Pituitary Basophilism)," which appeared in the *Bulletin of the Johns Hopkins Hospital* (50: 137-195, 1932). After discussing 12 cases he concludes:

A polyglandular syndrome hitherto supposed to be of corticoadrenal origin characterized in its full-blown state by acute plethoric adiposity, by genital dystrophy, by osteoporosis, by vascular hypertension, and so on, has been found at autopsy in six out of eight instances to be associated with a pituitary adenoma which in the three most carefully studied cases (Cases 6, 7, 10) has been definitely shown to be composed of basophilic elements, the lesion in one instance (Case 7) having been clinically predicted before its postmortem verification.

While there is every reason to concede, therefore, that a disorder of somewhat similar aspect may occur in association with pineal, with gonadal or with adrenal tumors, the fact that the peculiar polyglandular syndrome, which pains have been taken herein conservatively to describe, may accompany a basophil adenoma in the absence of any apparent alteration in the adrenal cortex other than a possible secondary hyperplasia will give pathologists reason in the future more carefully to scrutinize the anterior pituitary for lesions of similar composition.

R W B

MASSACHUSETTS MEDICAL SOCIETY
STATED MEETING OF THE COUNCIL

A stated meeting of the Council of the Massachusetts Medical Society will be held in John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, October 6, 1943, at 10 00 a.m.

Business

1. Call to order at 10:00 a.m.*
2. Presentation of record of meeting held May 24, 1943 (Published in the *New England Journal of Medicine*, issue of July 8, 1943.)
3. Reports of standing and special committees
4. Appointment of an auditing committee
5. Fill any vacancies in the offices of the Society
6. Such other business as may lawfully come before this meeting

MICHAEL A. TIGHE, M.D., Secretary

*It should be noted that the meeting will be called to order a few minutes earlier.

ADVANCE INFORMATION FOR THE COUNCIL

REPORT OF PROGRESS BY THE POSTWAR LOAN FUND COMMITTEE

The Postwar Loan Fund Committee was organized on June 16, 1943, with fifteen members appointed by the president, Dr. Roger I. Lee.

The second meeting of the committee of the whole was held on Wednesday, August 11, 1943, at 8 Fenway, Boston, at which time the reports of the five subcommittees appointed by the chairman to study certain phases of this problem were read by the chairman of each subcommittee and discussed by all members of the committee of the whole. This is a report of progress of the committee of the whole.

The first subcommittee (Dr. Peirce H. Leavitt, chairman) studied the following questions:

- (1) Amount of loan to be granted.
- (2) Whether or not interest is to be charged.
- (3) Whether or not endorsers will be necessary.
- (4) Length of time the loan may run.

The committee reported that it believes that the amount must, of course, be uncertain, but would depend on two factors: the amount of money raised by the Society and the need of the applicant. The committee expressed the opinion that just enough interest to remind the applicant that he had a loan and to cover the carrying charge should be collected — this interest not to exceed 2 per cent. The committee stated that in its opinion no endorsers should be asked from members of the Society, and further stated that the length of time the loan may run should be within a two-year period. The committee of the whole, after discussing this subcommittee's report, accepted these conclusions.

The second subcommittee (Dr. Walter G. Phippen, chairman) then reported on the questions studied by them:

- (1) Eligibility of persons to borrow money from the fund.
- (2) Whether or not physicians other than members of the Massachusetts Medical Society at the time of entering the armed services should be permitted to borrow from the fund.

The committee reported that it believed that only men who were members of the Massachusetts Medical Society when they entered the armed forces should be permitted to borrow from the fund. None of the members believed that the fund should be open to all physicians in Massachusetts. The committee of the whole discussed this report, and it was approved in principle.

The third subcommittee (Dr. Charles Wilinsky, chairman) considered the question whether the fund should be raised by:

- (1) Increasing dues.
- (2) Assessing members \$10 or more for one year.
- (3) Assessing members \$10 or more over a period of three to five years.

The committee reported as follows:

It is our considered opinion that these funds should be raised not by increasing the dues, but rather by an

annual assessment of \$10 for the duration of the war unless otherwise modified by future action of the Council.

The committee reported that the present by-laws of the Society make provision for such assessments and authorize the Treasurer to collect them. The report of this subcommittee was considered at great length by the committee of the whole, and the report was accepted in principle.

The fourth subcommittee (Dr. Herbert L. Lombard, chairman) reported on how best to inform the members of the Society in the armed forces of the availability of this fund. The committee reported as follows:

We unanimously agree on three points:

Information should be printed in the *New England Journal of Medicine*. There should also appear in a box on the cover of the *Journal* an announcement calling the article on the inside page to the attention of members.

Form letters should be sent to men in the armed services notifying them of this action by the Society.

Form letters should be sent to other members of the Society with the annual bills for dues, stating the availability of these loans.

This report was also accepted in principle by the committee of the whole after considerable discussion.

The fifth subcommittee (Dr. George Leonard Schadt, chairman) made a report on the question concerning the relation of the individual county district societies to the Society in developing and making the Postwar Loan Fund workable. The subcommittee believed that the fund should be administered from the headquarters of the Massachusetts Medical Society, rather than from the district societies, so that no member would be embarrassed in going to his district society and asking for a loan. It was also thought that a member desiring a loan would be more apt to ask for it if it were done through the headquarters of the Society. This question was also discussed at length and agreed to in principle by the committee of the whole.

GEORGE LEONARD SCHAT, *Chairman*

REPORT OF THE COMMITTEE ON PUBLIC RELATIONS

Congress has appropriated funds to provide medical, nursing and hospital maternity and infant care for wives and infants of enlisted men up to the seventh pay grade under plans developed and administered by state health agencies and approved by the chief of the Children's Bureau.

The Committee on Public Relations met in conference with Dr. Vlado A. Getting, state commissioner of public health, who discussed the administration of this plan in Massachusetts. In this state all deliveries will be in a hospital. All deliveries will be by graduates of Grade A schools or by those approved by a technical committee; the latter committee for the most part is identical with the Committee on Maternal Welfare of the Massachusetts Medical Society. Dr. Getting in this connection pointed out that a ruling by the Attorney General of the Commonwealth made it possible for the Department of Public Health to set standards for the care of the patients coming under this provision that are

different from those set by the Board of Registration in Medicine. In other words, the right to practice medicine in Massachusetts does not necessarily give the individual doctor the right to participate in this plan.

The service in Massachusetts will be limited to the wives and offspring of privates and the next three higher grades of enlisted personnel of the Army, Navy and Marines. The application for help, under this plan, must be signed by both the physician and patient.

The plan provides for the payment for consultations with other obstetricians, pediatricians and surgeons. These services are to be paid for without deduction from the sum agreed on in the original plan for obstetric care. The maternity benefit is limited to those who are willing to accept ward care in a hospital. The doctor is to be paid the sum of \$50 for the prenatal, the delivery and ordinary post partum care. Home visits are to be paid for at the rate of \$5 to \$10 for the first visit and lower fees for subsequent visits.

Hospitals within Metropolitan Boston are to be paid at the rate of \$450 a day, and those outside of this area at the rate of \$350 a day.

Dr Getting asked for the endorsement of this plan in principle only. The Committee on Public Relations endorses the plan in principle.*

Further information on this subject is contained on page 945 of the July 31, 1943, issue of the *Journal of the American Medical Association*.

ALBERT A. HORNER, *Secretary*

DEATHS

BRENNAN—JOHN J. BRENNAN, M.D., of Worcester died August 26. He was in his eightieth year.

Dr Brennan received his degree from Harvard Medical School in 1886, and later studied in Vienna and London. He was a member of the Massachusetts Medical Society and the American Medical Association and a former member of the State Board of Optometry.

His widow, two sons and a daughter survive.

DAUDELIN—S. ALPHONSE DAUDELIN, M.D., of Worcester, died August 28. He was in his seventy-fourth year.

Born in Sutton, P. Q., Dr Daudelin received his degree from Laval University, Montreal, in 1895. He was one of the original founders of the old Franco-American Dispensary, which was the parent of the former Louis Pasteur Hospital. In 1907, Dr Daudelin was appointed by President Theodore Roosevelt as high commissioner and plenipotentiary from the United States to France for a period of six months covering the Maritime Exposition. The French government awarded him the Cross of Knight of the Legion of Honor, and on the completion of his mission, Dr Daudelin remained in France for advanced study, specializing in eye, ear, nose and throat. He was elected to membership in several important French medical societies, and was named and served as head of the eye and ear clinic at Amiens, France. While in Paris, Dr Daudelin helped found the Comité Franco-Américain, an organization that now has branches in all leading cities in this country. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives.

*The Executive Committee at its meeting on August 25, 1943, knew of and filed the report in principle.

MISCELLANY

NOTE

Dr Harry C. Solomon has recently been appointed professor of psychiatry at Harvard Medical School and medical director of the Boston Psychopathic Hospital. He succeeds the late Dr C. Macfie Campbell.

AWARD TO GENERAL ELECTRIC X-RAY CORPORATION

Robert P. Patterson, Under Secretary of War, has recently announced a second award for excellence of war production to the General Electric X-Ray Corporation, of Chicago. This permits the company to add a white star to its Army-Navy E flag, which has flown over the plant since January 26 of this year.

BOOK REVIEWS

A Short History of Cardiology. By James B. Herrick, M.D. 8°, cloth, 258 pp., with 48 plates and frontispiece. Springfield, Illinois: Charles C. Thomas, 1942. \$3.50.

In this interesting resume of the history of cardiology, Herrick first reviews the period from Hippocrates to Harvey, and rightly calls attention to the fact that in the Hippocratic writings, although there is an interesting fragment on the anatomy of the heart, the only consideration of its function is the employment of the pulse in the estimation of fever, whereas the matter of the pathology is scarcely treated, in fact was practically unknown. Aristotle's mistake in attributing to the heart the functions of the brain is well known. Celsus was responsible for the confusion of disease of the heart with that of the cardiac opening of the stomach, the *morbus cardiacus*, which produced so much confusion for so many years.

The great Galen knew the anatomy of the heart, except for his fatal mistake about the pores in the septum, which kept him so far from the true explanation of circulation. Nonetheless, eminent authorities have said that he contributed more to our knowledge of the heart than anyone before Harvey. He proved by experiment that the arteries contained blood and not air, and the acuteness of his observations is shown by his discovery in the embryo of the ductus arterii and ductus botalli, of which, however, he had no conception of the function. He gave tremendous and even bewildering attention to the pulse, writing sixteen essays on that subject.

The author gives an interesting résumé of progress of knowledge of cardiology during the two hundred years preceding Harvey and rightly calls attention to the influence of important world events, such as the invention of printing and gunpowder, the fall of Constantinople and the discovery of America, on medicine in general and on cardiology in particular.

Leonardo da Vinci's influence on cardiology is adequately treated, and a drawing of his is reproduced that shows even the moderator band of the right heart. The contributions of Vesalius and the martyr Michael Servetus are well described. The next period includes Harvey to Laennec. The author truly says that no abstract of Harvey's work can do it justice. The story of the contributions and controversies of Columbus and Fabricius are well told. Facts about Lower, Mayow and Hales bring out the fascinating story of the gradual growth of knowledge by the scattered contributions of individuals.

Space allows details regarding the progress of

the story of cardiology down to present times; the parts played by all the great contributors are taken up in order and adequately discussed in a masterly fashion. The book throughout is characterized by a broad point of view. It is extremely well illustrated, with portraits of the principal participants in the march of science. The book is fascinating reading, and to him who seeks—and who does not—the history of an important part of medical knowledge, it can be most highly recommended.

Manual of Oxygen Therapy Techniques, including Carbon Dioxide, Helium and Water Vapor. By Albert H. Andrews, Jr., M.D. 12°, cloth, 191 pp., with 33 figures and 16 tables. Chicago: The Year Book Publishers, Incorporated, 1943. \$1.75.

This is a technical handbook rather than a medical textbook on gas therapy. Accordingly, only a little over four pages are given to the medical aspect of this subject. In the chapter entitled "Physiology of Respiration and Rationale of Inhalation Therapy," the author manages to clarify the mechanism of respiration in terms of ventilation, the transportation and absorption of oxygen, and the elimination of carbon dioxide. From an adequate oxygen supply, which is derived from normal breathing, the author passes over to the abnormal condition in which anoxia or "oxygen want" occurs. To relieve this oxygen deficiency, he suggests the use of gas therapy, employing oxygen, carbon dioxide, helium and water vapor.

The rest of the book is strictly technical and is therefore crowded with details, tables and figures. These relate to the purchase and maintenance of equipment from the standpoint of economy and efficiency, as well as the indications for use, the technic of application and the necessary precautions. In addition to the usual procedures, the author pays attention to certain exceptional cases. Thus, he gives specific instructions for this form of treatment when it is administered to infants in incubators or when it is to be carried out in the home, where hospital facilities are lacking.

The reviewer is not aware of the existence of an oversupply of texts on this subject. He is therefore of the opinion that this manual will prove to be a useful guide to those of the medical profession who are called on to administer gas therapy.

The Principles and Practice of Medicine: Originally written by Sir William Osler. By Henry A. Christian, M.D., LL.D., Sc.D. (hon.), F.R.C.P. (Can.). Fourteenth semi-centennial edition. 4°, cloth, 1475 pp. New York: D. Appleton-Century Company, Incorporated, 1942. \$9.50.

There is something appealing about meeting a book that is fifty years old and still young, that has gone through fourteen editions, each one successful, and that has kept alive a tradition of good medical writing through the hands of three different authors.

The fourteenth edition of Osler looks not unlike the first: the reviewer's copy of the first edition happens to be bound in green whereas the fourteenth is in red. But the two books can stand side by side companionably, as should all medical fathers and sons, the older book perhaps still able to show the younger something in the way of literary style. Youth in return now adds to the parent volume a full half century of new ideas, customs and medical knowledge.

When Dr. Christian took over the task of editing the

thirteenth edition of Osler he did this with a sympathetic understanding of what Osler had in mind. This edition appeared in 1938 and was at once well received by the medical reading public. That it was successful is proved by the fact that a new edition has been forthcoming so quickly.

The fourteenth edition begins with a chapter on functional diseases of the nervous system, an arrangement that might have made Dr. Osler smile. The book continues to be a complete handbook of internal medicine, up to date in every particular and continuing to have what, to the reviewer at least, is a particular charm—the even character of writing that can be found only in a one-man book. Each chapter has now appended a select group of references to important literature. Tropical diseases are discussed in a way that will appeal to all medical officers. On the whole, any student or practicing physician brought up with an admiration for Osler will feel that this textbook is still the proper one to use.

Clinical Anesthesia: A manual of clinical anesthesiology. By John S. Lundy, M.D. 8°, cloth, 771 pp., with 266 illustrations. Philadelphia and London: W. B. Saunders Company, 1942. \$9.00.

Dr. Lundy has contributed his wide experiences of over twenty-five years in the practice of anesthesia. They are mostly personal expressions gained at the Mayo Clinic. There is much controversial material in the book; however, the author is frank and honest in his statements, which are fortified by an experience probably unequalled by any anesthetist in the country.

Dr. Lundy deserves much credit for pioneering in the field of anesthesia, having established the use of many of the newer drugs and technics, and many of the procedures described in his book were originated by him. In the opinion of the reviewer, reference to the works and technics of contemporaries and mention of the variety of apparatus and equipment in universal use, together with more illustrations, would have given the reader a broader knowledge of modern anesthesia.

The book opens rather abruptly with the choice of anesthetic agents and methods. If the reader were introduced to the basic fundamentals of anesthesia and if the development of the subject matter followed in chronological sequence, it seems that a clear picture of anesthesia as a whole would be presented. The tabulation of anesthetic agents and methods according to the various surgical procedures is unique; comments in the text are referred to by interrogation points on the charts.

The following chapter, covering the use of local anesthetic agents, is well written and extremely valuable. It is the high light of the book for reference by anesthesiologists and surgeons.

The chapter on spinal anesthesia relates the author's personal experiences but does not enlighten the reader concerning the many advances made with agents other than procaine. More emphasis on this subject would have aided the reader. The author's opinions on complications and dosages are stressed.

The chapter on equipment and drugs is extremely well written with many suggestions of value.

The next seven chapters consider general anesthesia, the stages and signs of general anesthesia, preoperative and postoperative care, the agents employed for general anesthesia and the gaseous agents used for the support of respiratory function. It seems as though more refer-

ence could have been given to the technic of carbon dioxide absorption, which has revolutionized the administration of inhalation agents

Endotracheal or intratracheal anesthesia is well described as well as its many complications

The chapter on general anesthesia in dentistry and obstetrics barely covers two important fields of surgery that have been sadly neglected

The chapter on intravenous anesthesia is excellent, as might be expected, since the author has been responsible for pioneer work in this field The methods of rectal and oral intubation rate the few pages consistent with their position in anesthesia Balanced anesthesia, a term coined by the author, is mentioned in a two paragraph chapter

The chapter on anesthesia for nonsurgical conditions demonstrates the mystery of the author in diagnostic prognostic and therapeutic nerve blocks, procedures concerning which most physicians are relatively ignorant

The remaining chapters and the appendix cover venipuncture, intravenous therapy, resuscitation, records, the anesthetic statistics of the Mayo Clinic from 1924 to 1940 and the chemistry of analgesics and anesthetics, as well as a chronological table of anesthesiology and allied subjects and conversion tables of weights and measures

This book is well worth reading for reference to the experiences, impressions, and recollections of a pioneer physician and master in modern anesthesia

Diseases of the Liver Gallbladder and Bile Ducts By S S Lichtman, MD 8°, cloth, 906 pp, with 122 illustrations and 1 colored plate Philadelphia Lea and Febiger, 1942 \$11 00

This book is a great storehouse of facts and opinions about the liver and its diseases Its value is increased by a long list of well-chosen references at the end of each chapter The material is so varied and extensive that it is hard to single out special chapters for review

The book is well arranged starting with 100 pages on the structure and physiology of the liver, followed by about 50 pages on liver poisons, nutrition diet in protection and damage to the liver, the role of vitamins and the mechanism of jaundice In discussing jaundice only Rich's classification into retention and regurgitation types is described From the reviewer's point of view, McNee's classification of external obstructive, hepatocellular and hemolytic jaundice seems more useful

About 50 pages are given to the symptomatology of diseases of the liver the section is well arranged although the description of the various symptoms and signs is somewhat uneven in quality Regarding the spleen the practicing physician is probably more interested in the percentage that are palpable than that of those weighing more than 300 or 600 gm at necropsy

About 95 pages are devoted to a description of laboratory aids and liver function tests, all of which is valuable for reference Many of the fifty tests described are little used now and have only a historical interest The inclusion of so many tests is possibly confusing to the practitioner

Then follow about 400 pages covering specific diseases of the liver The author's classification of seven types of catarrhal jaundice seems rather elaborate in a disease in which necropsy is rare and their separation into two groups—with and without initial gastrointestinal symp-

toms—appears to be somewhat artificial Cirrhosis of the liver is given an especially complete description To list ten types of cirrhosis on one page is rather confusing but this disease is described under the familiar headings—portal biliary and pigment cirrhoses and Bant's disease In the jaundice of hepatocellular disease (catarrhal jaundice, toxic hepatitis, cirrhoses and so forth), the author seems to overemphasize the mechanical factor of obstruction within the liver and to minimize the poor excretion of bilirubin by the damaged lobular cells The chapter on the hepatorenal syndrome does not help much in clarifying this difficult subject The figures for the incidence of syphilis of the liver date back to a generation or two ago, when the diagnosis and treatment of syphilis were very different from what they are at present, it is now a relatively rare disease in the ward or at necropsy The incidences of the common types of jaundice differential diagnosis and diagnostic errors are given careful consideration

In addition to the paragraphs on treatment under the various diseases, a 25 page chapter is given to the treatment of liver disease in general this is sound and up to date but might well be enlarged at the expense of the many pages on laboratory procedures

The last 110 pages are devoted to diseases of the gall bladder and biliary passages

The author has drawn liberally on the best literature for facts, opinions tables and illustrations The paper, type and illustrations are excellent, as are many of the photomicrographs

Nasal Medication A practical guide By Noah D Fabricant MD 8°, cloth, 122 pp with 20 illustrations Bal timore The Williams & Wilkins Company 1942 \$2 50

This book is a practical guide not only for the specialist in rhinology but also for the general practitioner and pediatrician The author is associate in laryngology, rhinology and otology at the University of Illinois College of Medicine He has devoted considerable time to research in the physiology of the nasal mucous membranes and in the pharmacologic action of the common drugs used in nasal medication The book includes a brief section covering the anatomy of the nasal cavity and the paranasal sinuses, including both gross anatomy and histology He also discusses histopathology and nasal physiology In the latter subject the biochemistry of the nasal secretions is discussed and the hydrogen ion concentration of these secretions is described in considerable detail The significance of the latter has only recently been recognized and the author is one of the most enthusiastic contributors to this newer conception of nasal physiology A great deal of emphasis is laid on the effect of drugs on ciliary action it being considered particularly harmful to destroy or inhibit this action which is of tremendous importance in keeping the nasal mucous membrane free of foreign particles

Contrary to common belief menthol camphor and eucalyptol seem to have no beneficial effect in opening the nasal passages in fact menthol in some experiments has seemed to produce a narrowing of the nasal passages and an increase in the resistance to the stream of air passing through the nose The cooling action of menthol has probably caused patients to believe that there was a clearing of the airway The author adds Definite destructive changes throughout all layers of mucous membrane are produced by a 5 per cent solution of menthol

Ephedrine hydrochloride seemed to produce little if any change in the tissue, whereas epinephrine hydrochloride in dilutions of 1:1000 used over a long period of time caused considerable damage to the tissues.

It is recommended that, if aqueous solutions are used, they should be isotonic. There is a discussion of the use of oils as sprays or drops, including the possible complication of lipid pneumonia. A great deal has been written by many authors on the latter subject. This author summarizes the pros and cons. He quotes Wishart, who points out that there are really very few cases of lipid pneumonia when one considers the large amount of oil inhaled by an enormous number of people.

There are short discussions on the use of silver nitrate, zinc ionization, sodium sulfathiazole and Mercurochrome.

Finally, there is a complete description of methods of applying nasal medication. These include the displacement method of Proetz, the lateral-head low-posture method, Beck posture, nasal tampons, sprays, cotton applicators, inhalers, jellies and emulsions, irrigations and even snuffs. Irrigation of the sinuses is also discussed, and at the end there is a chapter on nasal medication in disease.

The book is clearly written. It is not too technical and is well documented. It gives a fair discussion of many controversial subjects. Its greatest value is a real attempt to place nasal medication on a scientific basis.

The Electron Microscope. By E. F. Burton, Ph.D., head of the Department of Physics and director of the McLennan Laboratory, University of Toronto; and W. H. Kohl, development engineer, Rogers Radio Tubes, Limited, Toronto. 8°, cloth, 233 pp., with 144 illustrations. New York: Reinhold Publishing Corporation, 1942. \$3.85.

No library should be without this extremely valuable book. The electron microscope is destined to play an increasingly important part in the newer experimental techniques that are to be applied in the field of biology, of which medicine is integral. The authors are to be congratulated on the readable style of their book. There are many instructive diagrams and plates, and a useful general bibliography is appended.

Contribucion al estudio anatomico clinico de las afecciones del endocardio. A doctorate thesis (Universidad Nacional de Buenos Aires, Facultad de Ciencias Medicas, No. 5636) by Manuel Perea Muñoz. 4°, paper, 363 pp., with 92 illustrations. Buenos Aires: "Esmeralda," 1942.

This thesis is simultaneously a brief review of the literature on endocarditis and an analysis of 206 cases of abnormalities of the endocardium in a series of 1000 autopsied cases studied since 1936 in the Laboratory of Pathological Anatomy, Ramos Mejia Hospital, Buenos Aires. Among these cases, there were 64 with valvular disease.

The twenty-five chapters in the book take up the classification of endocarditis and discuss acute and subacute bacterial endocarditis, syphilitic involvement of the endocardium, rheumatic endocarditis, "benign" endocarditis, endocardial atheroma and calcification, neoplastic disease and malformations, along with valvular defects.

The author's 206 cases are summarized under the headings of the various chapters. Of 44 cases of bacterial endocarditis, 15 are said to have been the result of sepsis, 4 are labeled terminal, 5 acute bacterial, and 20 subacute

bacterial. Fifty-four cases on a rheumatic basis are also summarized, 36 in men and 18 in women. Thirteen cases of syphilitic involvement of the endocardium are included, as well as 41 cases of atheroma of the endocardium and 27 of valvular sclerosis. A few congenital defects are also added, but they can hardly be classed as true endocardial disease.

The volume presents detailed studies of this rather small group of cases, but the lesions are so varied and the cases in the different categories are so few that statistically the volume is of little importance and it seems larger than necessary for presentation of these data. The chief value of the book lies in the individual case reports, which are worthy of perusal. The volume is well printed and the illustrations are good. There is a short bibliography.

Effects of Alcohol on the Individual: A critical exposition of present knowledge. Volume 1. *Alcohol Addiction and Chronic Alcoholism.* Edited on behalf of the Scientific Committee of the Research Council on Problems of Alcohol by E. M. Jellinek, Sc.D. 8°, cloth, 336 pp., with 43 tables and 5 figures. New Haven: Yale University Press, 1942. \$4.00.

The Research Council on Problems of Alcohol, a recent organization, has been extremely active. Under the chairmanship of Dr. Karl M. Bowman, and with a board of men, most interested in this problem, it has fostered research and issued an excellent journal, *The Quarterly Journal of Studies on Alcohol*, from the Laboratory of Applied Physiology, Yale University.

This book is a survey of the general problems with extensive bibliographies. The book is divided into sections on alcoholic addiction, mental disorders associated with alcoholism, studies on vitamin deficiencies, the encephalopathies, cirrhosis of the liver and Marchiafava's disease. In these finely written chapters, one has at hand an up-to-date account of each subject, thoroughly documented, with the literature carefully analyzed. Much of this literature, incidentally, was collected by Dr. Merrill Moore, under the direction of the Works Progress Administration.

The book can be highly recommended as a comprehensive review of the subject, as a reference work and as a basis for studies on an acute problem, particularly important in wartime.

Surgical Physiology. By Joseph Nash, M.D. 4°, cloth, 496 pp., with 16 illustrations. Springfield, Illinois: Charles C Thomas, 1942. \$4.00.

This book is based on lectures given by the author at New York University College of Medicine as part of a graduate course in surgery. As indicated by the title, aspects of physiology that are of especial importance in surgery have been emphasized. The text is written in a clear, concise manner. The book is divided into seven sections dealing with the following subjects: the circulatory system, the respiratory system, the alimentary system, the body fluids, the endocrine glands, the cerebrospinal nervous system and the autonomic nervous system. There is an excellent list of references dealing essentially with the more recent contributions of physiology to surgery.

This book should make a strong appeal to the practicing surgeon and to the postgraduate student.

(Notices on page xii)

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ENDEMIC ROCKY MOUNTAIN SPOTTED FEVER IN MASSACHUSETTS

A DANIEL RUBENSTEIN MD * AND HAROLD F ROWLEY, MD †

BOSTON AND HYANNIS, MASSACHUSETTS

ALTHOUGH Rocky Mountain spotted fever has been reported from all geographical regions in the United States,¹ it was not recognized in New England prior to 1937, when 2 cases were discovered in Rhode Island² and 1 in Massachusetts.³ From that time until 1942 at the end of the so called 'tick season' 8 cases were reported from four of the six New England states: Massachusetts, 4, Rhode Island, 2, Connecticut, 1, and New Hampshire, 1. The source of infection of 3 of these cases was found to be in regions outside of New England. The 5 remaining cases originated in Massachusetts, which is apparently the sole New England state where the disease is endemic.

All 5 Massachusetts infections were acquired on Cape Cod. Four cases were attributed to three contiguous communities comprising an area of fifty nine square miles. It must be borne in mind that all endemic Massachusetts cases occurred during the three year interval from 1937 to 1939, and that this disease has not reappeared on Cape Cod since 1939.

The distribution according to the month of onset of the Massachusetts cases was as follows: May, 1, June, 1, July, 3. The dog tick, *Dermacentor variabilis*, which is the vector of this disease in the East, becomes most plentiful during the latter part of May or early in June, and declines sharply after mid July.⁴ There is usually a lag of several weeks between the time of maximum abundance of ticks and the peak in case incidence.

Of the 5 cases endemic in Massachusetts, 3 have been reported previously.^{2,3} This paper will include a discussion of the two remaining cases. From one of these the causative virus was recovered⁵ and has been maintained by serial passage in guinea pigs. The isolation of this virus has

presented the only opportunity to study the endemic agent responsible for Rocky Mountain spotted fever in Massachusetts.

CASE REPORTS

CASE 1: R. E., a 4 year-old boy, was admitted to the Children's Hospital on June 5, 1939, with complaints of difficulty in walking and fever of 1 week's duration. He came from Cape Cod, where he had been bitten by several ticks during the 3 weeks before admission. He had been well until 1 month before admission, when he developed a limp for which a local physician could find no explanation. Nine days before entry, he became irritable and the temperature was found to be elevated. He complained of severe headache and joint pains so severe that he was unable to stand. Two days later a rash appeared, beginning on the wrists and ankles and spreading to the trunk, neck and face. The temperature remained elevated throughout the week before admission.

On admission the temperature was 101.2°F, the pulse 100, and the respirations 20. There was moderate generalized adenopathy. Although limitation of motion was noted in the shoulders, wrists, fingers and ankles, no outward changes could be detected. There was a generalized maculopopular eruption (Figs 1 and 2). The lesions were discrete and measured from 2 to 3 mm in diameter, they were present on the head, neck, trunk and extremities, including the palms and soles. The remainder of the physical examination revealed no other abnormality.

Urinalysis was essentially negative. The red-cell count was 3,600,000, and the hemoglobin 90 per cent (Sahli). The white-cell counts ranged from 20,000 on admission to 8600 on June 14. Blood smears were normal. Lumbar puncture on June 6 showed no abnormal findings. Tuberculin tests on June 6 and June 8 were negative. A blood culture taken on June 5 was negative. A blood Hinton test on June 5 was negative. A Weil-Felix reaction on June 5 was positive in a dilution of 1:5120. Electrocardiograms on June 7 and 14 were not remarkable. Chest plates on June 5 and 7 showed slight peribronchial congestion.

The patient was drowsy and apathetic during the first 2 days. The temperature remained elevated during this time and became normal on the 3rd hospital day.

We are indebted to Drs. R. Earl M. Smith and John A. V. Darr of the Children's Hospital for permission to publish this case report.

*State Director of Health, Office of Communicable Diseases, Massachusetts Department of Public Health.

†Member, Medical Service, Cape Cod Hospital, Hyannis, Massachusetts.

though it rose to just above 100°F. on one or two occasions thereafter. The pulse averaged 120 for several days. The rash gradually disappeared and had faded completely

vere frontal headache, which persisted for several days. There was gradually increasing restlessness, irritability and a whimpering cry at night. On the 4th day of the

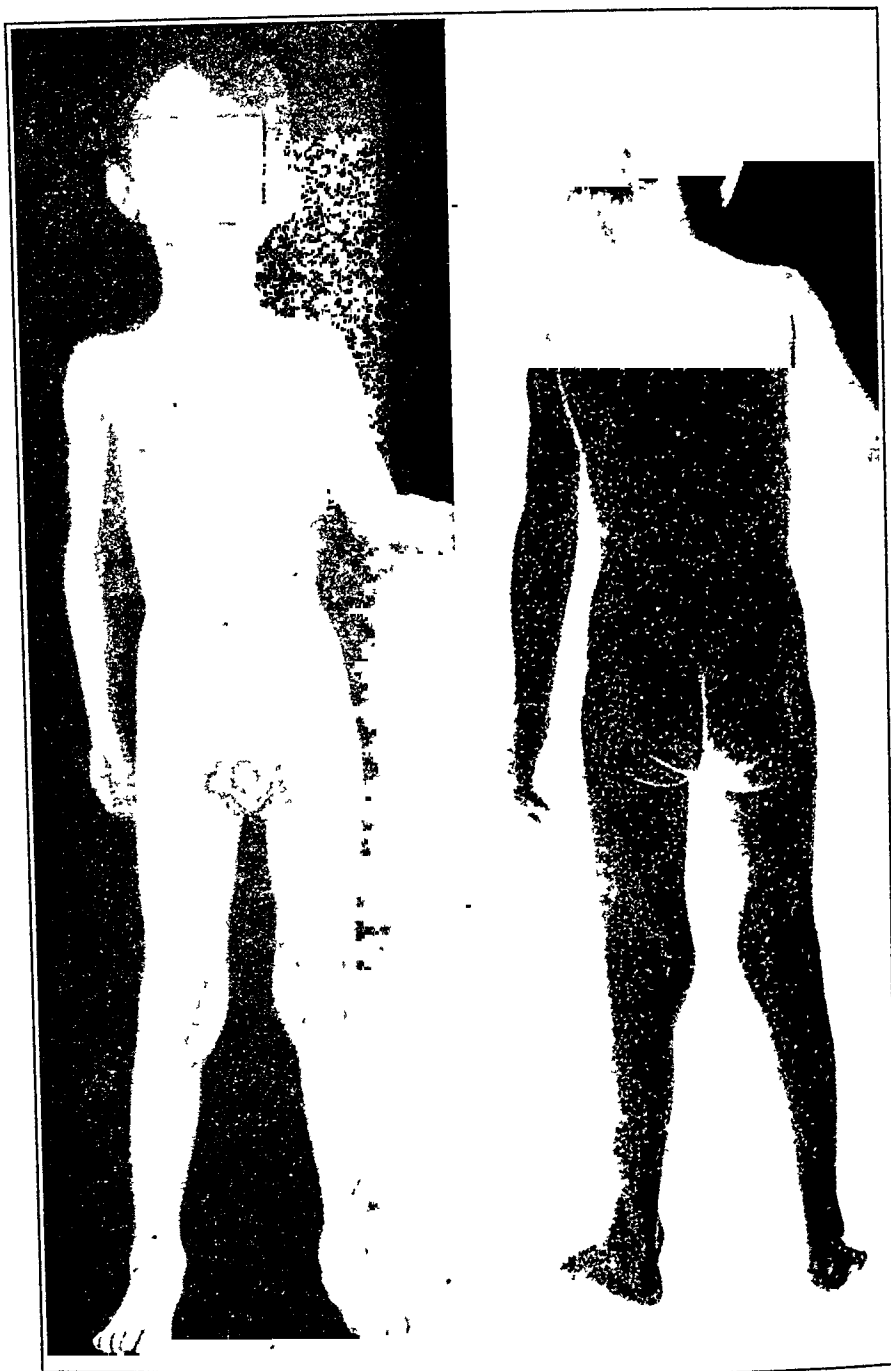


FIGURE 1. Case 1.

The photographs show the generalized maculopapular eruption.

at the end of a week. Recovery was uneventful, and the joint complaints had disappeared completely at the time of discharge.

CASE 2. M. E. S., an 8-year-old girl residing in Dennis, Massachusetts, was admitted to the Cape Cod Hospital in Hyannis on June 12, 1938, with complaints of headache, fever and malaise. She had been well until 5 days previous to admission, when she began to complain of se-

illness, a macular eruption appeared on the buttocks and spread to the arms, legs and face. The temperature during the first 5 days of the illness varied between 99 and 105°F. At times the patient was irrational. The past history was not contributory; there had been the usual childhood diseases. Seven siblings and the parents were living and well.

On admission the temperature was 100.8°F., and the pulse 120. Physical examination revealed a well nourished

child lying apathetically in bed. The face was dusky. Except for an eruption on the skin, the examination was negative. Maculopapular lesions were generally distributed over the face, forearms, both buttocks and the labia majora. These lesions were discrete in some areas and confluent in others, and faded on pressure.



FIGURE 2 Case 1

This photograph shows the eruption on the soles of the feet

Urinalysis showed varying degrees of albuminuria from June 12 to July 12. The red-cell count, which was 4,500,000 on admission, gradually dropped to 2,600,000 on July 6. Hemoglobin determinations ranged from normal levels at admission to 45 per cent (Sahli) early in July. The white-cell count rose from 7200 on June 12 to 23,000 on June 16. During the subsequent months it fell slowly to about 12,800. Differential counts were not unusual except for a moderate increase in polymorphonuclear leukocytes to about 85 per cent during the first 10 days of the illness. A blood culture taken on June 21 was negative. A lumbar puncture on August 1 revealed a clear fluid, no increase in pressure and a total cell count of 34 lymphocytes. The blood chemical findings were normal. A lumbar puncture on September 2 showed no abnormalities. Electrocardiograms were reported as follows: June 26, PR interval of 0.16 second, July 26, sinoauricular tachycardia and a PR interval of 0.20 second, October 12, PR interval of 0.16 second and a high take off of the ST interval in Leads 1 and 2. The serologic studies* were as follows: The Weil-Felix reaction was positive in dilutions of 1:320 on June 15, of 1:640 on June 22 and of 1:320 on July 4. On June 22, the agglutination reaction with a rickettsial antigen was positive in a dilution of 1:640, and on February 15, 1943, a complement fixation test for Rocky Mountain spotted

fever was positive in a dilution of 1:128 and one for endemic typhus was negative. On June 15, 1938, 3 cc of blood was inoculated at the bedside into two guinea pigs. The infectious agent was isolated from each animal.

The rash noted on admission gradually faded and was replaced on the 8th day of the illness by a generalized petechial eruption somewhat accentuated on the wrists, ankles and upper back. There were few lesions on the face and the anterior aspect of the trunk. On June 17, a nonpitting edema was noted on the face, eyelids and feet. The rash, which had been bright pink, assumed a darker hue. In some areas where the eruption appeared to be most hemorrhagic the lesions coalesced to form large purplish blotches. These were most prominent over the wrists and feet. Three days later the rash became more extensive as a fresh crop of petechiae appeared.

The irritability noted on admission persisted. Although stuporous at times, the patient could be aroused to respond to questions. She gradually lapsed into coma. There was evidence of increasing involvement of the central nervous system. The pupils became dilated and did not react to light. There was slight weakness of the left side of the face. Control of the vesical and anal sphincters was lost. From day to day there was considerable variation in the neurological signs. Having lost the ability to take food by mouth, the patient was fed by gavage, and this had to be continued until October 16. She remained comatose for about 3 months. During this period no voluntary muscular movements could be detected. On August 6, the patient began having numerous attacks of opisthotonos lasting from a few minutes to several hours. These attacks recurred for 3 weeks. During the latter part of September movements of the fingers and arms were first noted. Feeding by stomach tube was discontinued as the swallowing reflexes were restored. Mental recovery was slow. On October 27, the patient spoke for the first time in 4 months. At discharge on December 7, she was alert mentally, although she still spoke in a whisper.

Beginning June 22, extensive sloughing of the skin was noted. This continued until a considerable proportion of the body integument was involved, including the skin of the left leg, left mid thigh, both knees and the extensor surface of the upper and lower thirds of the right thigh. These areas healed quite slowly and were eventually the sites of extensive scar tissue formation.

On July 29, the course was further complicated by intermittent attacks of acute pulmonary edema. During these episodes the pulse became rapid, and auscultation revealed coarse rales throughout both lung fields.

During the early part of the illness the temperature and pulse were markedly elevated, the temperature on June 24 having been recorded as 106°F (axillary). Fever of considerable degree persisted until late in September, a period of 3 months. From October to November it varied from 98° to 101°F and it gradually became normal late in November. The pulse level corresponded in general with that of the temperature. The total duration of elevated temperature was 5½ months.

Shortly after discharge, the patient was able to stand alone for the first time in several months. As mental improvement continued, she was soon able to read and write. She was readmitted in August, 1939, because of difficulty in walking owing to contracting scar tissue in the region of the sacrum and both thighs. There was marked

*The agglutination tests were performed by Florence K. Fitzpatrick, Ph.D., of Sharp and Dohme Incorporated, Clendinning, Pennsylvania, and the complement fixation on tests by Dr. I. A. Bengtson of the United States Public Health Service.

relief following plastic surgery of the skin. In 1942, the patient's mentality had been completely restored.

Bacteriologic data. The infectious agent was recovered by intraperitoneal inoculation of guinea pigs with blood from the patient taken on the 8th day of the illness. In subsequent studies, the incubation period of the disease in the guinea pig was about 5 days.⁶ The agent was apparently not exceedingly virulent for guinea pigs, since there were no fatalities among any of the inoculated animals. Although all the guinea pigs reacted to the injection of the agent by showing elevation of temperature, only 30 per cent of them showed noticeable scrotal swelling. All the animals that recovered were found to be solidly immune when reinoculated with a virulent strain of Rocky Mountain spotted fever. The isolated agent was effectively neutralized by convalescent serum obtained from the patient. Animals already immune to Rocky Mountain spotted fever did not react to inoculation with the agent.

Convalescent serum obtained 4½ years after onset of the disease in 0.5-cc. and 0.25-cc. amounts neutralized completely a Bitter Root Valley strain of Rocky Mountain spotted fever virus.⁷ Control animals receiving the same virus together with normal human serum died of the disease.

DISCUSSION

Since 1931, when the identification of Rocky Mountain spotted fever in the eastern part of the United States⁸ led to the discovery of numerous cases in that region, it had been held that this disease was more fatal in the West than in the East. Laboratory data supported this idea for several years. Strains isolated in the West were more virulent for guinea pigs than were those recovered in the East. During 1940, however, Topping and Dyer⁹ were successful in isolating from a patient in Washington, D. C., a highly virulent strain of Rocky Mountain spotted fever virus that had many characteristics of the most virulent strains obtained from Bitter Root Valley, Montana. According to the reactions of this virus in guinea pigs,—that is, the duration of the incubation period, the ability to produce fatal disease, and the scrotal lesions,—the Washington strain was highly virulent. Furthermore, in 1941 a strain of low virulence was recovered from a case in Wyoming.¹⁰ Statistical studies had already shown that when fatality rates of Eastern and Western cases were arranged according to comparable age groups, apparent differences between them vanished.¹¹ Hence, the terms "Eastern" and "Western" when applied to Rocky Mountain spotted fever had lost their former significance.

The strain isolated in Massachusetts, when judged by the usual criteria, was of low virulence. However, the clinical course of the patient from whom the virus was isolated was by no means mild. Actually this case presented clinical findings ordinarily associated with the severest type of infection. Marked involvement of the central

nervous system with coma, opisthotonos, muscle tremors and severe cutaneous manifestations, such as a confluent hemorrhagic eruption followed by necrosis and sloughing, is found in most fulminating cases.¹² The patient in Case 2 showed all these findings. Moreover, the prolonged hyperpyrexia and severe mental disturbance offer additional evidence of an exceedingly severe infection.

Rumreich, Dyer, and Badger¹³ in 1931 observed that disturbances of the central nervous system in Rocky Mountain spotted fever are often severe. Wollbach,¹⁴ discussing the pathology of this disease, described focal brain lesions often associated with thrombosis of small blood vessels and necrosis. Hassin¹⁵ described a fatal case in an eleven-year-old girl who, in addition to coma and a confluent hemorrhagic rash, presented signs of meningeal irritation including rigidity of the neck, a positive Kernig sign and a count of 10 cells in the spinal fluid. The histopathology at post-mortem examination was described as a nonsuppurative meningoencephalitis. Although spinal-fluid findings in cases of Rocky Mountain spotted fever are usually within normal limits, pleocytosis is occasionally noted. Carey¹⁶ in 1939 reported 2 cases with spinal-fluid counts of 24 and 224 cells, respectively; the smear in the second case revealed 12 per cent polymorphonuclear leukocytes and 88 per cent lymphocytes. A third case presented xanthochromic fluid. Apparently central-nervous-system manifestations of Rocky Mountain spotted fever are at times an integral part of the clinical picture.

Patients may exhibit varying degrees of edema. As in Case 2, this occurs during the acute stage of the illness. Parker¹⁷ observed that albuminuria is frequently encountered and that complete urinary retention may occur. Ong and Raffetto¹⁸ analyzed 18 cases in children and noted edema in 4 of them. In 2 cases the edema was generally distributed, and in the other 2 it was local, affecting the hands and feet in one patient and the face and feet in the other. The exact cause of this edema, which is usually nonpitting, has not been established. One might postulate a marked reduction in serum protein as a possible explanation. No studies concerning this aspect of the disease could be discovered in the literature.

The early diagnosis of Rocky Mountain spotted fever depends primarily on the evaluation of the available clinical data. Unfortunately, all serologic tests are negative during the first week of the disease. It was recently stated that the Russians have developed a method by which typhus fever can be diagnosed on the second or third day.¹⁹ No details concerning this test have as yet been revealed. Isolation of the Rocky Mountain spotted fever virus must be performed early in the disease before lysis has occurred. This proce-

dures, however, is lengthy, and there is considerable delay before the etiologic agent is definitely identified. The Weil-Felix reaction, using various strains of the genus *Proteus*, has been useful in the diagnosis of rickettsial disease after the first week of illness. This test, however, does not distinguish between typhus fever and Rocky Mountain spotted fever. Epstein²⁰ in 1922 and Zinsser and Castañeda²¹ in 1932 showed that convalescent serums agglutinate rickettsial antigens. Fitzpatrick and Hampil²² observed that in infected rabbits the development of rickettsial agglutinins precedes that of *Proteus* agglutinins. Recently Bengtson and Topping²³ demonstrated the value of the complement-fixation test in the diagnosis of rickettsial infections. They suggested that this test can be used in the differential diagnosis of Rocky Mountain spotted fever and typhus fever. In cases of typhus fever significant titers are obtained by this test on the ninth and tenth days after onset. The reaction remains positive for many years after recovery. Thus, in Case 2 a positive complement-fixation test for Rocky Mountain spotted fever in a dilution of 1:128 was obtained four and a half years after onset. The complement-fixation test for typhus fever was negative.

The only laboratory confirmation of the diagnosis of Rocky Mountain spotted fever in Case 1 was the Weil-Felix reaction. However, the history of several tick bites, the clinical picture and the positive agglutination reaction leave little doubt concerning the diagnosis.

Recently Topping²⁴ found that monkeys and guinea pigs survived experimental inoculation with the virus of Rocky Mountain spotted fever following the administration of a hyperimmune rabbit serum. Tissues of infected ticks were used as the antigen in the preparation of this serum. Kurotchkin, von der Scheer and Wyckoff²⁵ then showed that an effective serum results from injecting rabbits with rickettsiae cultivated in the yolk sac according to the method of Cox.²⁶ Newer methods used in the cultivation of rickettsiae have facilitated considerably the development of rickettsial vaccines and therapeutic serums.^{6, 26, 27} The successful use of serum in the treatment of experimentally infected animals has suggested its application to human cases of Rocky Mountain spotted fever. Such a therapeutic serum is now available commercially.* It is to be expected that this form of treatment should be most effective early in the course of the disease, before the serologic tests become positive. Hence, familiarity with the clinical signs and symptoms of Rocky Mountain spotted fever is important.

A prophylactic vaccine made from the tissues

of infected adult wood ticks (*D. andersoni*) has been available for many years.²⁸ Field studies performed in the West with this killed vaccine have demonstrated that it has definite immunizing value. In 1937, Bengtson²⁹ reported protection against infectious doses of the Rocky Mountain spotted fever virus in guinea pigs previously immunized by a formalized rickettsial antigen prepared from infected guinea-pig tissues grown in tissue culture. Cox,³⁰ in 1939, demonstrated the protective value for guinea pigs of vaccine prepared from rickettsiae cultivated in embryonic chick tissue. In Massachusetts the risk of acquiring Rocky Mountain spotted fever, even in the endemic area, is so small that routine prophylactic inoculation is scarcely justifiable.

The possibility of the future occurrence of Rocky Mountain spotted fever in Massachusetts merits careful consideration. At first glance some reassurance may be derived from the failure of any new cases of Massachusetts origin to appear since 1939. In 1935, Parker,³¹ however, called attention to the tendency of this disease to occur in cycles. Hence, in some local endemic areas in the West, intervals between cases were sometimes quite prolonged. In one county the disease disappeared for nine consecutive years only to reappear. This phenomenon is particularly likely to occur in regions similar to the endemic area in Massachusetts, where Rocky Mountain spotted fever exists in a localized region.

It is odd that Massachusetts remained free of this disease until 1937. Although the clinical manifestations of Rocky Mountain spotted fever are striking, experience in other states has demonstrated that the disease frequently goes unrecognized.¹³ It is now well known that prior to 1931 these cases were often labeled "endemic typhus." Investigation of the records of the Massachusetts Department of Public Health did not, however, bring to light any similar confusion. Observations in the West have shown that the virus of Rocky Mountain spotted fever can exist for many years in the ticks of a given area without the occurrence of the disease in man.³² Later, owing to some factor as yet unknown, the disease suddenly makes its appearance.

Although thousands of persons are exposed to ticks each spring and summer throughout Cape Cod and its adjoining islands, the paucity of cases of Rocky Mountain spotted fever indicates that the proportion of infected ticks is small. Of the three species of ticks concerned in the natural transmission of the disease, two varieties are present on the Cape; namely, the dog tick (*D. variabilis*) and the rabbit tick (*Haemaphysalis leporispalustris*). Surveys conducted in 1938 showed that

*Manufactured by the Lederle Laboratories, Incorporated, Pearl River, New York.

although the dog tick is found throughout the New England states, it is most plentiful on Cape Cod and the islands of Martha's Vineyard, Nantucket and Naushon.⁴ In the East, only the dog tick causes the transmission of the disease to human beings. The rabbit tick, which does not bite man, is important in the maintenance of the virus in nature and is only indirectly involved in the occurrence of the disease in man.⁵

There are several factors that help to maintain and propagate the virus in nature. Experimental work with *D. andersoni* has demonstrated that the infectious agent, once acquired by the immature forms of the tick, is passed on to the adult stage.³³ The agent is also transmissible through the ova of infected females. Furthermore, when infected immature or adult forms of the tick feed on a susceptible host, this host becomes infected, and other ticks that feed on this host during the infectious stage may acquire the virus.¹⁷ Studies with *D. variabilis* have suggested a similar method of transmission.³⁴

It might be argued that the endemicity of Rocky Mountain spotted fever in Massachusetts is a temporary and perhaps accidental occurrence rather than a natural phenomenon, and that the virus was brought into this area by infected ticks on dogs, these ticks in turn transmitting the virus to native Massachusetts ticks. Another possible avenue of introduction is by means of the rabbit tick. For many years rabbits have been imported into the Cape for hunting purposes. Parker³⁵ has postulated that in the West the virus of Rocky Mountain spotted fever passes from infected rabbit ticks to previously uninfected wood ticks through the rabbit, a host common to both species. Although the adult dog tick is rarely found on the rabbit, the accession catalogue of the United States Bureau of Entomology and Plant Quarantine, reveals that the immature forms are more frequent on the rabbit.⁴ A similar mechanism may be assumed in the East. On the other hand, the simultaneous appearance of Rocky Mountain spotted fever throughout widespread areas in the East suggests long-standing endemicity rather than a gradual spread from one region to another. Nevertheless, the situation in Massachusetts, where relatively few cases have been discovered, may not be entirely analogous to that in other Eastern areas where the disease is more prevalent. No matter how the virus was introduced into Massachusetts, the occurrence of future cases is not a remote possibility. A marked increase in prevalence is, however, extremely unlikely. An awareness of this disease on the part of physicians may disclose additional cases.

SUMMARY

Eight cases of Rocky Mountain spotted fever have been reported from four New England states from 1937 to 1942. Five of these cases had their origin in Massachusetts during the three-year period of 1937 to 1939. The total endemic area in Massachusetts comprises only fifty-nine square miles.

Two cases of Rocky Mountain spotted fever are presented. From one of these the infectious agent was recovered, this being the only case of Massachusetts origin thus far reported from which the virus has been isolated. Neutralizing antibodies were demonstrated in the blood of this patient four and a half years after recovery.

Absence of cases in Massachusetts since 1939 does not necessarily imply a disappearance of the virus, since epidemiologic data acquired in the West demonstrate that the disease may vanish from a localized endemic area for several consecutive years, only to recur.

Although the occurrence of Rocky Mountain spotted fever in Massachusetts may have been the result of an accidental and perhaps transitory introduction of the infectious agent from outside sources, there is a possibility that the virus may have existed here for many years. The relatively few cases suggest that only a small proportion of the ticks on Cape Cod harbor the infectious agent.

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THE ASCORBIC ACID CONTENT OF LATE-WINTER TOMATOES*

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THE tomato is generally considered one of the most important of the protective foods, owing largely to its vitamin C content. It is commonly classed as a vitamin C food and is frequently listed as one of the richest natural sources of ascorbic acid (vitamin C). Since it can be raised easily even by amateur gardeners, it is almost universally recommended for the home garden. It is also grown in enormous quantities for commercial canning, and for the manufacture of tomato juice. As a result of this extensive use and great popularity of the tomato, many studies have been made of its ascorbic acid content.

Apparently a number of factors affect the amount of ascorbic acid developed in tomatoes. For instance, Tripp, Satterfield, and Holmes¹ found varietal differences ranging from 14.8 mg. per 100 gm. for John Baer tomatoes to 21.8 mg. for Pritchard, and MacLinn and Fellers² report values varying from 9.0 mg. for Pritchard Stokes to 59 mg. for Princess of Wales (Sutton). The reports by Booher, Hartzler and Hewston,³ Curran,⁴ MacLinn, Fellers and Buck,⁵ Hamner and Maynard⁶ and others who have carefully reviewed the literature indicate that field-grown, fully ripened, vine-matured, summer tomatoes contain about 25 mg. of ascorbic acid per 100 gm. Thus a good-sized tomato of this type could supply nearly half the 75 mg. of ascorbic acid recommended by the Committee on Food and Nutrition of the National

Research Council⁷ for the daily needs of the human adult.

One frequently finds on the market, however, tomatoes that in neither color, taste nor physical appearance compare with the high quality of the field-grown, vine-matured summer tomatoes. Such tomatoes are commonly found in the stores of the northeastern United States during the late winter and early spring months. Inasmuch as these tomatoes are grown, shipped and sold under conditions quite different from those of the normal, local growing season, it appeared desirable to determine the ascorbic acid content of typical late-winter tomatoes. Such data are of particular interest to the physician, nutritionist and homemaker who wish to ascertain accurately the amount of ascorbic acid supplied by late-winter tomatoes, and the present study was conducted to accumulate these data.

The tomatoes analyzed were obtained from six local stores. Three of these were of the small private or independent type and three were representative of the large chain grocery stores. The tomatoes were purchased in small retail packages or by the pound, just as a homemaker would purchase them for home use.

Samples for analysis were obtained by cutting slices, weighing 10 to 15 gm., through the medial section in the same manner as the tomato is prepared for serving. The assay procedure described by Tripp, Satterfield and Holmes¹ was followed. The skin was quickly removed and the slices immediately submerged in acetic acid and thoroughly macerated by grinding in a mortar with acid-washed sand. Thus, destruction of vitamin C by enzymes was reduced to a minimum. The mix-

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TABLE 1. *The Ascorbic Acid Content of Late-Winter Tomatoes.*

MONTH OF PURCHASE	STORE	WEIGHT PER TOMATO	COST PER POUND	ASCORBIC ACID CONTENT	WEIGHT REQUIRED TO YIELD 75 MG. OF ASCORBIC ACID	COST OF 75 MG. OF ASCORBIC ACID
		gm.	cents	mg./100 gm.	gm.	cents
February	Chain A	—	29	8.0	938	60
		93.7	29	4.0	1876	120
		Average	29	6.0	1407	90
March	Chain A	84.3	29	5.4	1389	89
		92.1	29	7.0	1071	68
		88.1	29	8.0	938	60
March	Independent A	Average	29	6.8	1133	72
		130.6	36	5.9	1271	101
		92.4	36	7.4	1014	80
March	Independent A	111.0	36	4.4	1705	135
		77.1	36	5.2	1442	114
		Average	36	5.7	1358	108
April	Independent B	96.0	18	6.7	1119	44
		90.4	18	9.8	765	30
		103.4	18	7.6	987	39
April	Independent B	82.0	18	17.5	429	17
		Average	18	10.4	825	33
April	Independent C	85.6	33	7.3	1027	75
		93.7	33	9.5	789	57
		101.7	33	8.8	852	62
April	Independent C	65.0	33	8.4	893	65
		102.4	33	12.0	625	45
		Average	33	9.2	837	61
April	Chain B	74.6	35	10.2	735	57
		75.5	35	12.9	581	45
		113.4	35	4.8	1563	121
April	Chain B	111.0	35	9.4	798	62
		Average	35	9.3	919	71
April	Chain A	84.4	29	8.1	926	59
		88.3	29	8.0	938	60
		116.7	29	7.3	1027	66
April	Chain A	81.7	29	9.9	759	48
		—	29	7.6	987	63
		Average	29	8.2	927	59
April	Independent A	102.4	42	16.0	469	44
		48.2	42	10.5	714	66
		93.0	42	13.9	540	50
April	Independent A	59.0	42	12.7	590	55
		71.7	42	14.1	532	49
		Average	42	13.4	560	53
April	Chain B	75.1	32	8.6	872	61
		86.8	32	13.0	577	41
		93.1	32	10.2	735	52
April	Chain B	84.4	32	11.8	636	45
		75.8	32	10.3	728	51
		Average	32	10.8	710	50
April	Independent B	83.0	32	10.8	710	50
		77.4	29	6.1	1229	79
		98.7	29	7.1	1056	68
April	Independent B	105.4	29	10.7	701	45
		84.8	29	13.2	568	36
		90.9	29	5.2	1442	92
April	Independent B	Average	29	8.5	999	64
		91.4	29	8.5	999	64
April	Chain C	71.6	33	6.2	1210	88
		77.5	33	2.5	3000	218
		79.3	33	2.5	3000	218
April	Chain C	100.3	33	3.1	2419	171
		74.7	33	5.8	1293	94
		Average	33	4.0	2184	158
April	Independent C	80.7	33	4.0	2184	158
		105.9	30	9.1	824	54
		93.1	30	9.2	815	54
April	Independent C	95.1	30	4.9	1531	101
		98.3	30	8.3	901	60
		94.2	30	6.0	1250	83
April	Chain C	Average	30	7.5	1064	70
		97.3	30	7.5	1064	70
		98.4	30	5.0	1500	99
April	Chain C	82.6	30	6.9	1087	72
		89.5	30	14.1	532	35
		96.3	30	7.6	987	65
April	Chain C	76.3	30	22.0	341	23
		57.1	30	12.4	605	40
		Average	30	12.4	605	40

ture of finely ground tomato, acetic acid and sand was transferred to a centrifuge tube and spun at 2000 r.p.m. for ten minutes, which produced a clear supernatant liquid. The ascorbic acid content of this liquid was obtained by titration with sodium-2, 6-dichlorophenolindophenol dye to a faint-pink end point.

The results obtained from the assay of 58 tomatoes are reported in Table 1, which also includes data concerning the source, weight and cost, the amount of tomato required to yield 75 mg. of ascorbic acid and the cost of this amount from the tomatoes in question. The average weights of the tomatoes obtained at the thirteen purchases were 93.7, 88.2 and 92.8 gm. for chain store A, 93.6 and 83.0 gm. for chain store B, 80.7 and 83.2 gm. for chain store C, 102.8 and 74.9 gm. for independent store A, 93.0 and 91.4 gm. for independent store B and 89.7 and 97.3 gm. for independent store C. The average weight of all the tomatoes was 88.8 gm. The cost per pound varied from 18 cents for the first purchase from independent store B to 42 cents for the second purchase from independent store A.

The ascorbic acid content of the tomatoes is reported on a 100-gm. basis. It varied widely within each of the thirteen lots as well as between the lots. The average values were 6.0, 6.8 and 8.2 mg. for chain store A, 9.3 and 10.8 mg. for chain store B, 4.0 and 11.3 mg. for chain store C, 5.7 and 13.4 mg. for independent store A, 10.4 and 8.5 mg. for independent store B and 9.2 and 7.5 mg. for independent store C. The average ascorbic acid content of all the tomatoes was 8.8 mg. per 100 gm. The lowest value obtained was 2.5 mg., and the highest was 22.0 mg. for tomatoes purchased from chain store C. This latter value, and a few of those obtained for other tomatoes, are similar to those obtained by a number of investigators for field-grown tomatoes, but the average ascorbic acid content of the late-winter tomatoes, 8.8 mg. per 100 gm., is only about one third that of summer tomatoes. In fact, it is definitely less than the ascorbic acid content of canned tomatoes, which are available at the time late-winter tomatoes are consumed. Daniel and Rutherford⁸ found that the ascorbic acid content of tomatoes canned six months previously was 14 mg. for glass containers and 15 mg. for tin containers. Rogers and Mathews⁹ compared commercial and home-canned tomatoes and found 13.8 mg. of ascorbic acid for the former and 13.9 mg. for the latter. Hence, it is obvious that whereas the late-winter tomato possesses attractive decorative features for the table, particularly in salad combinations, it does not have the ascorbic acid

value of fresh summer tomatoes or of tomatoes canned six months previously.

Obviously, tomatoes cannot be relied on as the sole source of ascorbic acid in the dietary. Nevertheless, for the sake of comparison, an estimation has been made of the amount of these tomatoes that would be required to supply the 75 mg. of ascorbic acid recommended by the Committee on Food and Nutrition of the National Research Council⁷ for daily consumption by adult man. The lowest amount of tomato required was 341 gm., or about three quarters of a pound, and the maximum amount required was 3000 gm., or approximately 6½ pounds. It is clear from these values that late-winter tomatoes as ordinarily eaten in the average home can contribute only a small portion of the daily human requirements for ascorbic acid.

The cost of the quantity of tomatoes required to contribute 75 mg. of ascorbic acid to the diet varied from 17 cents for a purchase at independent store B, to \$2.18 for tomatoes purchased from chain store C. The average costs for 75 mg. of ascorbic acid in the thirteen purchases of tomatoes were 90, 72 and 59 cents for chain store A, 71 and 50 cents for chain store B, \$1.58 and 56 cents for chain store C, \$1.08 and 53 cents for independent store A, 33 and 64 cents for independent store B and 61 and 70 cents for independent store C. The average cost of 75 mg. of ascorbic acid from the late-winter tomatoes was 72 cents. It is interesting to compare this cost with 4.8 cents reported by Holmes, Patch and Tripp¹⁰ for 75 mg. of ascorbic acid obtained from oranges available at the same season of the year. Obviously neither the tomatoes nor the oranges would be consumed solely for their ascorbic acid content, but on this basis it is significant that the ascorbic acid content of the late-winter tomatoes cost fifteen times as much as ascorbic acid supplied by oranges purchased at the same season of the year.

CONCLUSIONS

It is quite evident from the results of this study that the homemaker, nutritionist and physician must not consider late-winter tomatoes as equivalent to vine-matured, sun-ripened summer tomatoes as a source of ascorbic acid for the human dietary. In computing the vitamin C value of a diet containing late-winter tomatoes, one should not assign to them more than one third the ascorbic acid value ordinarily used for fully ripe, summer tomatoes.

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THE INCIDENCE OF GALLSTONES IN THE HIGHER AGE GROUPS*

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THE post-mortem records of the Long Island Hospital have been examined for the purpose of determining the incidence of gallstones in the higher age groups. The Long Island Hospital is designed for the medical care of the destitute of the City of Boston. The majority of its patients belong to the higher age groups and most of them are of Irish extraction; a minority are of Italian origin and a few are Negroes.

The post-mortem records, 3242 in all, for the years 1900 to 1942, inclusive, were studied with reference to the frequency of gallstones in relation to age, sex and lesions of the gall bladder, and to the question of an increase of cholelithiasis in recent decades.

The results yield only minimum figures because all post-mortem protocols without definite statements regarding the presence of gallstones were listed as negative. Cases of choledocholithiasis were listed as positive because the gall bladder is generally regarded as the sole source of concretions in the extrahepatic bile ducts.

Table 1 shows the incidence of gallstones found in 2791 post-mortem examinations of patients above the age of forty. The incidence increases with age. Below the age of forty, in 451 post-

stones. This steady rise in incidence of gallstones with age (by decades) has been reported by many authors (Crump,¹ Hansen,² Hamilton,³ Gross,⁴ Jaffé,⁵ Ludlow,⁶ Mosher,⁷ Naunyn,⁸ Ophüls⁹ and Scheel¹⁰) but has been denied by a few (Hesse and Hesse¹¹ and Ryerson¹²). Belief that cholelithiasis originates at a much earlier period, to become manifest in later life only, finds no support in the Long Island Hospital figures.

Table 2 presents figures regarding the association of gallstones and grossly manifest disease of the gall bladder. These are minimum figures because allowance has to be made for the incompleteness of many of the post-mortem protocols

TABLE 2. Incidence of Gall-Bladder Disease in Cases with Gallstones.

AGE	CASES WITH GALLSTONES			PERCENTAGE WITH GALL-BLADDER DISEASE		
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL
yr.						
41-60	40	65	105	37.5	26.1	30.4
61-80	162	221	383	45.0	36.2	40.0
81 and over..	40	56	96	37.5	35.7	36.5
Totals	242	342	584			37.5
General averages				42.1	34.2	

and for the varying degree of competency of the persons who made the examinations. Most of the lesions recorded were acute or chronic cholecystitis, fibrosis or hydrops of the gall bladder. There were a few cases of carcinoma (2 in males and 2 in females). Little attention was found to have been paid to cholesterosis of the gall bladder. However, the fact that only 38 per cent of all diseased gall-bladders containing calculi showed easily recognizable gross lesions corresponds with other reports—Scheel¹⁰ reporting 33 per cent of gall bladders with lesions and Ophüls⁹ (post-mortem material) 38 per cent. These low figures cast some doubt on the surgical dictum that there are no innocent gallstones. Cholecystitis without gallstones was found in about 2.5 per cent of the post-mortem examinations.

TABLE 1. Incidence of Gallstones, 1900-1942.

AGE	NUMBER OF CASES			PERCENTAGE WITH GALLSTONES		
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL
yr.						
41-60	475	340	815	8.4	19.1	12.9
61-80	975	708	1683	16.6	31.2	22.8
81 and over..	154	139	293	26.0	40.3	32.8
Totals ...	1604	1187	2791			20.9
General averages				15.0	28.7	

mortem examinations, the incidence was 1.5 per cent. Above the age of eighty, more than a third of the post-mortem examinations revealed gall-

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A definite sex difference in the incidence of gallstones, with ratio of almost 2:1 in favor of women, is evident from Table 3. This is lower than the ratios reported by many authors for Europe and the United States: Jaffé²⁵ gives about 3:1, Mitchell¹³ 3.5:1, Courvoisier¹⁴ 3:1, Brockbank¹⁵ above 2.5:1 and Hurst¹⁶ 5:1. However, Schretzenmayr,¹⁷ of Vienna, Gross,⁴ of Leeds, England, and Hamilton,³ of Adelaide, Australia, give a 2:1 ratio, and Ludlow's⁶ Lakeside Hospital (Cleveland) ratio of less than 2:1 corresponds most closely to that reported here. The higher incidence in women has often been attributed to the influence of pregnancy. The marked rise in incidence above the age of fifty (Fig. 1) does not support such a view

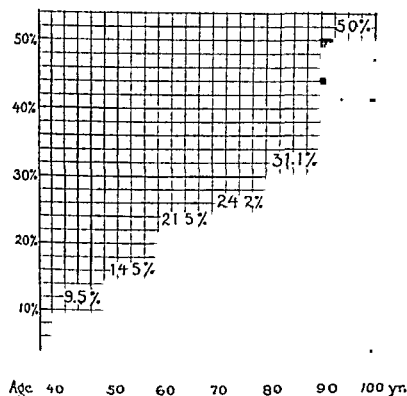


FIGURE 1. Incidence of Gallstones at Autopsy in Patients over Forty Years of Age.

and this is also the case with the reports of Scheel,¹⁰ Gross,⁴ Hamilton³ and Lichtwitz.¹⁸

Comparison of the presence of gallstones in the post-mortem material of the Long Island Hospital from 1900 to 1922 and 1923 to 1942 (Tables 3 and 4) shows a definite increase for the latter period.

TABLE 3. Incidence of Gallstones, 1900-1922.

Age	NUMBER OF CASES			PERCENTAGE WITH GALLSTONES		
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL
yr.						
41-60	204	233	437	4.4	17.6	11.4
61-80	260	355	615	13.0	29.8	22.8
81 and over	39	61	100	23.0	31.1	28.0
Totals	503	649	1152			18.9
General averages				10.3	24.5	

This increase involved all age groups above forty years and both sexes. The tendency of the sex difference to decrease in recent years is indicated

not only by these findings but also by a comparison of the older literature with publications of recent date. Because of the great variation in incidence of cholelithiasis recorded from different countries,

TABLE 4. Incidence of Gallstones, 1923-1942.

Age	NUMBER OF CASES			PERCENTAGE WITH GALLSTONES		
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL
yr.						
41-60	271	107	378	11.4	22.4	14.6
61-80	715	353	1068	17.6	32.5	22.6
81 and over	115	78	193	27.2	46.8	35.2
Totals	1101	538	1639			22.2
General averages				17.0	32.7	

only figures collected in the same general region are truly comparable. From Chicago, Mitchell¹³ in 1918 gave a 3.5:1 ratio, and Jaffé²⁵ in 1933 a 3:1 ratio. From Cleveland, Ludlow⁶ in 1930, gave a ratio of less than 2:1. The reports of Gross⁴ and Hurst¹⁶ indicate a similar shift for England.

A high incidence of gallstones is supposed by some authors, including Mosher,⁷ to occur in poorly nourished populations. Others, including English,¹⁰ maintain the contrary. The material reported here seems to favor the first view, but from lack of comparable material from higher income groups this question is left undecided.

SUMMARY

The data obtained from post-mortem records at the Long Island Hospital show that the incidence of gallstones increases with age.

Cholecystitis was present in 42 per cent of the males and 34 per cent of the females who had gallstones.

Cholecystitis without gallstones was found in 2.5 per cent of the cases.

A higher incidence of gallstones was found in the 1923-1942 period than in the 1900-1922 period.

The sex difference in incidence of gallstones has decreased in recent years.

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CLINICAL NOTE

KINEPLASTIC AMPUTATION OF THE FOREARM

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KINEPLASTIC amputation for the utilization of muscle power to activate a prosthesis is

the indifference and disfavor with which this method was received some thirty years ago. This procedure has a special value at the present time because it may play a leading part in the rehabilitation of those injured in the war.

The purpose of reporting the present case is to emphasize some of the points brought out by Kessler in his various articles. The report also carries a plea to surgeons who do original am-

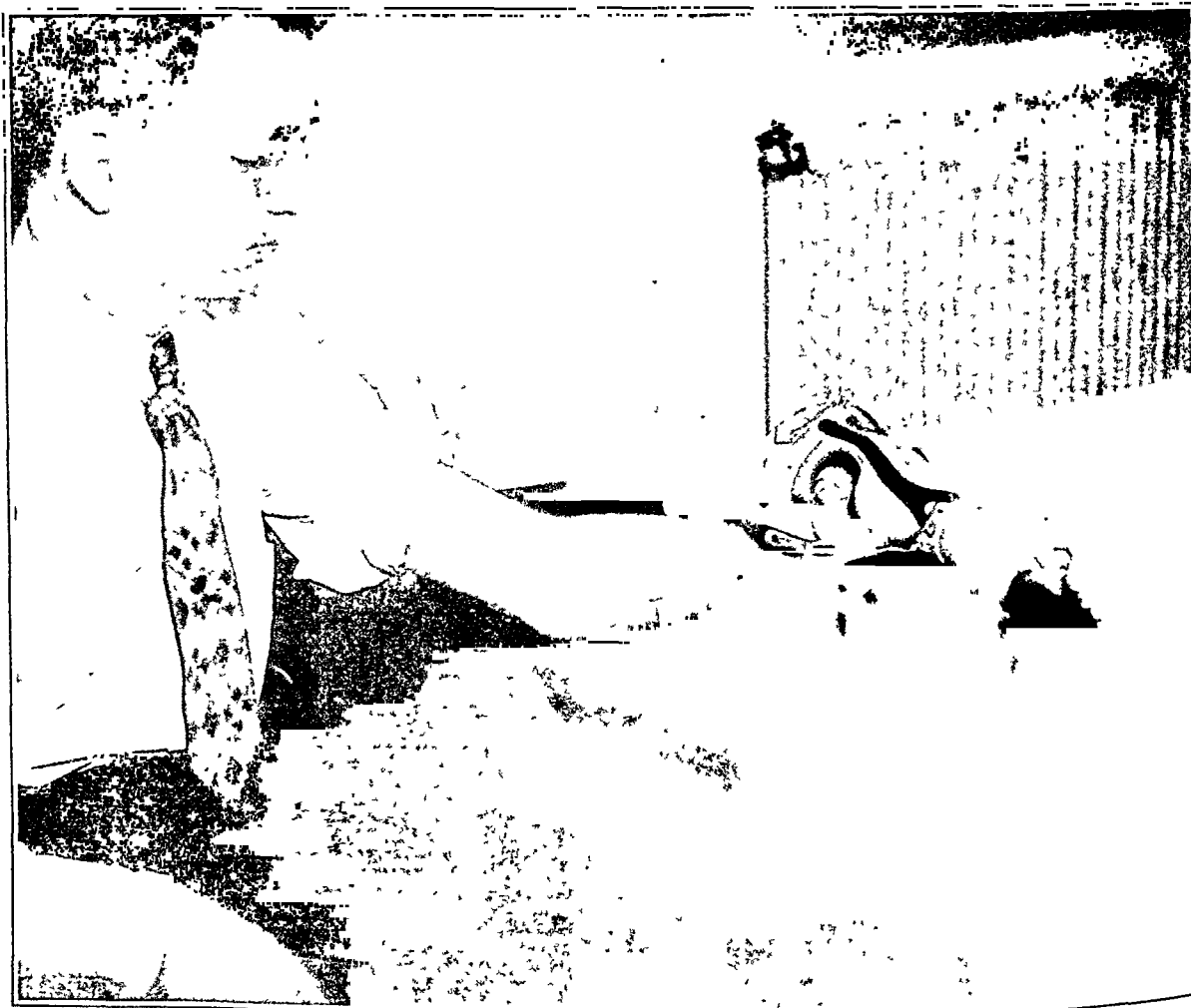


FIGURE 1.

This photograph shows the pins in place, with the prosthesis removed.

not a new procedure. Credit for it is due to Kessler,¹ whose work has done much to counteract

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putations to bear in mind the possibility that some type of prosthesis will be worn on the stump. In many cases one sees an attempt to save too

much of the arm, thus leaving a stump that will not adapt itself to any type of prosthesis. As a result, reamputation becomes necessary.

The technic of kineplastic amputation as described by Kessler, although comparatively simple,

The only way in which the value of this operation can be shown to a patient is to demonstrate a successful case. The study of photographs and reading matter will not convince him. He must be taught the precise limitation of function that

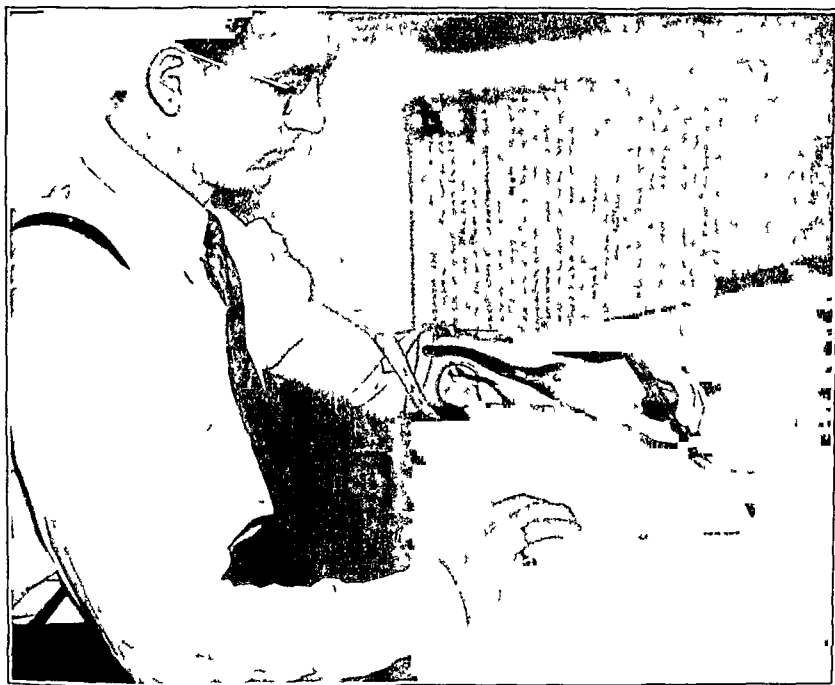


FIGURE 2

In this photograph the prosthesis has been attached. Note the wishbone and the mechanics of the prosthesis.

requires care and precision in several points, as follows:

- 1 The skin flap should not be over 35 cm square, otherwise there is likely to be some irritation from the pins. Also, one should not pass the skin tube through too much of the muscle belly, and the tendons should of course be avoided.

- 2 The edges of the skin tube should be carefully closed before it is canalized through the muscle.

- 3 Excess tension in closing the skin flap should be avoided.

- 4 The prosthesis should not be applied until all symptoms of discomfort and redness have disappeared from the skin tube.

will result from the amputation, and the decision whether it is to be performed should be left to him. The patient must be made to understand that the success of this procedure lies in complete co-operation. To become proficient in adapting oneself to the mechanical principles of a prosthesis takes time and patience. A course of education in the use of the involved muscles should be carried out in the interval between amputation and attachment of the prosthesis.

There are many handicapped people with amputations of the forearm who through years of effort have adapted themselves to devices of every kind, such as hooks and appliances, and who would be unwilling to forsake them for such a procedure as this. Such persons should not be allowed to demonstrate their appliances to the patient until

he has had an opportunity to see all types of prostheses and devices and to make his own selection among them. Kineplastic amputation has a definite place in such a selection.

CASE REPORT

A. G., a 21-year-old mill hand, was referred by Dr. Harold Kurth, of Lawrence. On October 9, 1941, he caught his left hand in a carding machine. It was practically stripped of soft tissue, and all the bones of the hand sustained multiple comminuted compound fractures. It was impossible to identify the tendons, so that amputation was decided on. This consisted in an ordinary flap amputation, which left a stump measuring 20 cm. from its distal end to the tip of the acromion. The flexor and extensor muscles were fastened to the ends of the amputated radius and ulna and the fascia to give anchorage for flexion and extension. Convalescence was uneventful and the patient returned to work in 3 weeks.

Having heard of Kessler's kineplastic amputation, he asked me to perform one. He was instructed to exercise the stump, going through the motions of closing and opening the fingers so as to develop and train the muscles of the forearm. He was most co-operative and did this religiously.

On March 26, 1942, the kineplastic amputation was done. Two flaps were marked out according to the Kessler technic. The dressing was not changed for 10 days. The skin grafts, which were small, took well. On

May 7, measurements were taken and a cast was made, pins having been left in the skin tube for the previous 2 weeks. On July 13, the prosthesis was attached.

At the present time, the patient is working full time. He has become proficient in manipulating his fingers, and is able to pick up his dinner pail, a suitcase, and a cigarette and to hold playing cards in his hand. In other words, following the application of the prosthesis he has learned to activate the artificial fingers with the muscle motors of his forearm as though he had his own fingers. The only complication was a slight irritation of the skin at the edge of the skin tube, which was probably due to the flap's having been made a little too large.

SUMMARY

Kineplastic amputation of the forearm by Kessler's technic is advocated as a valuable and successful procedure.

Complete co-operation of the patient is essential, and there should be preliminary training and exercise of the muscles of the forearm to facilitate function after the attachment of the prosthesis.

A successful case of kineplastic amputation is reported.

43 Bay State Road

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MEDICAL PROGRESS

CANCER: RESULTS OF TREATMENT*

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THERE is still a conviction among the laity and some of the medical profession that cancer cannot be cured or controlled. This pessimism exists in spite of extensive and convincing evidence to the contrary. It is a well-accepted fact that present-day treatment is effective in the early stages of the disease, before it has spread to distant organs or tissues that are essential to life. Moreover, the prognosis is far from hopeless even in more advanced cases. Unfortunately, however, a large proportion of the patients reporting for treatment are still in far-advanced stages. As was stated in a previous report,¹ powerful weapons are available that, if used judiciously and intelligently, will do much to control the disease. Naturally, all look forward to the discovery of an agent that will have a specific action or will enable the body to over-

whelm the cancer cell, but even if such an agent is found, it is apparent that it cannot be expected to cure all the cases. In the absence of specific treatment, one should not assume a defeatist attitude regarding present-day therapy, especially since reports in the last several decades reveal an increasing number of cures.

The present report deals with the probability of cure of the commonest forms of neoplastic disease. Although no attempt has been made to review the entire literature of the last ten years, it is hoped that the material cited represents the major contributions. It is a herculean task to evaluate critically each end-result study, but fallacies and discrepancies will be discussed so far as possible. The main purpose is to point out that cancer is a controllable disease; the figures that represent a cross section of the results in the large clinics throughout the world (Table 1) attest to this fact.

Certain fundamental concepts must be defined in order to understand and evaluate the reported statistics. First, what is a cancer cure? It is com-

*The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas, 1942. \$5.00).

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monly said that cancer is never completely cured, even though it may remain quiescent. In the case of certain lesions this may be true. However, autopsy findings on patients who die of other diseases and who have no clinical sign of cancer seldom reveal any active disease. Thus, clinical freedom from demonstrable disease must be accepted as the criterion. Perhaps the terms "clinical cure," "free of disease" and "survival without disease" are more applicable. Secondly, what period of time should elapse before one is justified in reporting a

life expectancy of the patients thereafter is essentially the same as that of the normal population. On the other hand, late recurrences of such lesions as cancer of the breast, ovary and so forth are notorious, thus making a ten-year period more desirable.

In the evaluation of end results many other factors must be considered. Foremost is the natural history of the untreated lesion, for without knowledge of this, the efficacy of treatment cannot be judged.²⁻⁴ The period in which the cases were

TABLE 1. *Reported Five-Year Curability Rates in Common Types of Malignant Neoplasm.*

ORGAN OR TYPE	CURABILITY RATE %	ORGAN OR TYPE	CURABILITY RATE %
Skin	48-68	Gastrointestinal tract:	
Basal cell	38-74	Stomach:	
Epidermoid	39-56	Absolute	5
Breast:		Relative	15-30
Absolute	22-28	Colon:	
Relative	30-51	Absolute	29
Oral cavity:		Relative	38-61
Lip	59-70	Rectum:	
Buccal mucosa	26-31	Absolute	25
Gingivae	27	Relative	38-73
Lower	15-60	Urinary tract:	
Upper	33-74	Bladder	16-55
Palate	23-38	Kidney	19-33
Hard	44*	Male genital tract:	
Soft	20*	Penis	35-40
Tongue	14-37	Testicle	15-53
Floor of mouth	18-32	Prostate:	
Tonsil	15-32	All cases	8
Respiratory tract:		Operable	50-58
Pharynx:		Female genital tract:	
Nasopharynx	18-30	Vulva	26-32
Metapharynx	15	Vagina	30
Hypopharynx	6-12	Cervix	20-40
Larynx:		Endometrium	35-45
Operable		Operable (surgery)	48-70
Laryngofissure (early cases)	80	Operable and inoperable (radiation)	35-45
Total laryngectomy	55	Ovary	16-35
Inoperable	27	Sarcomas:	
Thyroid gland:		Malignant melanoma	22-42
Early cases	70	Fibrosarcoma	18
All types	26	Osteogenic sarcoma	19-39

*Three-year rate.

clinical cure? Authorities throughout the world have agreed on an arbitrary elapsed time of freedom from disease for five years after the last treatment as a reasonable period to warrant the publication of statements regarding control of the disease. It should be realized that cancer is usually a disease of old age and that a number of patients who remain free of cancer die of intercurrent disease before the prescribed time for reporting the results of treatment. It must be pointed out, also, that in certain cancers a shorter interval is reliable, whereas in others longer periods are necessary. For example, a three-year survival without evidence of cancer is sufficient for lesions involving the oral cavity, since few cases recur after that time and the

treated is important, since methods of therapy, especially radiation, have improved markedly in the past twenty years. The stage of disease at the time the patient first comes for treatment alters end results considerably, since some clinics receive a much higher proportion of early cases than do others. Other points of major significance are the histologic criteria of cancer defined by the examining pathologist, the criteria of operability in the various clinics and the judgment and skill of the therapist in choosing and performing the most efficacious form of treatment in the given case. Finally, the method of calculation of end results is probably the greatest single factor in accounting for the differences in the reported figures. Many

clinics report the absolute cure rate—that is, the percentage of the total number of patients examined who are alive and free from recurrence after a stipulated number of years. All patients who are lost to follow-up examination, whether or not they had disease when last seen, and those who die of intercurrent disease before the specified period are counted as dead of cancer. Untreated and hopelessly advanced cases that receive only palliative therapy are also included in the totals. Since this does not give a true index of the efficacy of treatment, but merely denotes the prognosis for the particular lesion, other methods of reporting have been used. The commonest is the so-called “relative cure” or “determinate cure,” but the definition is variable from clinic to clinic. Some clinics include every patient except those who are not treated or who are lost immediately after treatment; others exclude patients in whom no attempt at cure was made, or who were lost to follow-up (even though free of disease), or who died of intercurrent disease. To report that patients were free of disease “from one to ten years” is of little value unless the actual number per year is stated. Even then, recurrence is frequent in the few years after treatment, and inclusion of cases recently treated to increase the number in a reported series is merely confusing. In many instances, a selected group of cases treated by specific methods is published, and this information is of value only in judging the efficacy of such therapy. Thus, it can be seen that reports cannot be directly compared unless the series are of similar composition and the methods of calculation the same. It is obvious that all the above factors must be considered before one can pass final judgment on any single report.

SKIN

Cancer of the skin is curable in a high percentage of cases, since the lesions are easily detectable and accessible to therapy by any of the accepted methods. The reports in the literature give credence to this thesis. Magnusson⁵ reports three-year cures in 76 per cent of cases of verified skin cancer, as against 75 per cent of those diagnosed clinically. The results in all cases were 75 per cent three-year and 55 per cent five-year survivals without disease. Warren, Simmons and Rea⁶ report freedom from disease in clinically diagnosed cancer of the skin without biopsy as 57 per cent for three years and 48 per cent for five years. However, they state that only 16 per cent of the patients were known to be living with cancer or had died from it. Of the remainder, 19 per cent died of intercurrent disease and 16 per cent were lost to follow-up. These are included as failures. As they point out, if the latter two groups, who were free of disease, are included as

cured, the survival rate becomes 84 per cent. It is also of interest that in this age group the expected mortality from natural causes is about 25 per cent within the five-year period. Thus, it is impossible to compute the actual curability rate of all patients who enter the clinic.

Histologic Type and Grade of Malignancy

The histologic type and grade of malignancy definitely alter the prognosis of the disease. Basal-cell cancer seldom if ever metastasizes, whereas metastases in epidermoid or squamous-cell cancer are not infrequent. Schuermann⁷ reports 74 per cent five-year cures in basal-cell cancers and 45 per cent in epidermoid cancers of the skin. The absolute cure in 401 cases of both types was 68 per cent and the relative cure 85 per cent. Poppe⁸ had three-year cures of 73 per cent and 55 per cent in basal-cell and epidermoid cancer, respectively, and 87 per cent in mixed types. McDowall⁹ states that in his series 234 (60 per cent) of 390 cases of epidermoid cancer and 310 (70 per cent) of 440 cases of basal-cell cancer were free of disease, but this refers only to primary healing and does not give the true end results. Warren and Hoerr¹⁰ reported 39 per cent five-year cures for epidermoid cancer, of which 44 per cent were in low-grade and 24 per cent in high-grade lesions. The mortality rate from cancer only was 27 per cent in low-grade and 51 per cent in high-grade lesions. The combined mortality rate from cancer only was 32 per cent, whereas the remainder, who were not included as cured, either died of intercurrent disease, were observed for less than five years or were lost before the specified period. Warren, Gates and Butterfield¹¹ studied the various types of basal-cell cancers and found 38 per cent five-year cures. The method of reporting was similar to that used in a previous study.⁶

Clinical Type and Site of Cancer

Halberstaedter and Simons¹² pointed out that if the lesion was superficial the curability was 83 per cent, but if it was infiltrating the rate dropped to 37 per cent. The survival rate in lesions of the exposed portions of the skin, such as the face and hands, is generally higher than in those elsewhere.^{10, 13}

BREAST

Most end-result studies deal only with operable lesions, so that the actual prognosis for all cases is considerably lower than that usually reported. The criteria of operability as well as the methods of therapy vary in the different clinics. Other factors are important, such as the stage and histologic type of the disease and the tendency for the lesion not only to invade the lymph nodes but to metastasize to distant organs. However, the re-

sults in any operable series are sufficiently good to warrant optimism regarding the treatment. In treatment, some clinics use surgery or radiation alone, whereas others combine the methods in various ways. The value of supplemental radiation is still debatable, but there should be no question concerning the type of surgical procedure to be performed. Some writers^{14, 16} have suggested that simple mastectomy alone or perhaps combined with radiation gives results comparable to those in lesions treated by more radical operations. The reasoning is based on observations of a highly selective group of patients, poor follow-up studies and fallacious suppositions. These writers maintain that the prognosis is so poor in the presence of lymph-node metastases that there is little to be gained by rigorous therapy. The results of therapy in the leading clinics completely refute these arguments. In the first place, the operative mortality of radical mastectomy is seldom more than 2 to 3 per cent, so that on this score alone one cannot justifiably withhold the radical operation. Secondly, the curability rate by radical surgery in cases with axillary metastases is sufficiently high to prove conclusively that it will save many lives. Thirdly, the clinical appraisal of axillary metastases is notoriously fallible and the curability by any method of radiation is exceedingly low. Consequently, one cannot be sure that simple mastectomy will completely eradicate the disease even in the absence of clinically demonstrable metastases. Fourthly, it is essential to remove the pectoral muscles even in the absence of axillary disease, since they are sometimes invaded by the tumor. Fifthly, the proportion of patients entering any clinic with axillary metastases and even more advanced disease is much higher than that of patients in whom the lesion is confined to the breast alone.

It has been found that in untreated cases approximately 15 per cent of the patients were still living six years after the discovery of the disease.^{2, 4} The delay in therapy in a study of cases treated before the last decade averaged about a year; it is less at the present time. The life expectancy from onset of over 1500 cases in all stages and treated from either a curative or a palliative standpoint reveals that 28 per cent were still alive six years after onset.⁴ Hence, taking all cases into consideration, therapy of any kind seems to improve the prognosis. However, the figures improve still more when only the operable lesions, treated by appropriate radical measures, are considered. In contrast to many types of cancer, those of the breast have a tendency to produce late metastases. Consequently, for ideal end-result studies at least a ten-year period should elapse after treatment. The five-year

however, give an accurate index of the prognosis of the treated lesion.

Five-year end results for operated cases range from 30 to 51 per cent¹⁰⁻³²; the absolute curability for all patients who have treatment of any kind (palliative or curative) is 22 to 28 per cent.^{4, 21} When the disease is confined to the breast, the five-year survivals range from 55 to 80 per cent and the ten-year survivals from 36 to 70 per cent. Involvement of the axillary nodes lowers the curability, but the rate is still far from poor. Representative results range from 18 to 45 per cent for five years and from 9 to 18 per cent for ten years. The extreme rates are unusual, for in most cases the results are about midway between them. The radical operation is fairly well standardized, so that except in those clinics where less radical procedures are carried out, the differences in results are due in large part to the criteria of operability. Thus, it can be easily seen that the radical operation is to be preferred and that it should be carried out whenever possible in spite of the fact that a few highly selected cases do almost as well by less radical measures. The merits of radiation alone or in combination with surgery have been reviewed by Brunschwig.³³ He concluded that the possible beneficial effects of preoperative radiation are vitiated by the morbidity resulting from the subsequent operation in a field so irradiated. He further stated that there was no evidence that postoperative radiation increases the survival rate if the disease is confined to the breast, but that it may possibly increase the rate in cases with axillary lymph-node involvement.

ORAL CAVITY AND RESPIRATORY TRACT

The degree of curability in cancers of the oral cavity and respiratory tract varies considerably with the site of origin of the primary lesion. In general, those lesions that arise in the anterior portion have a much higher rate of cure than those situated more posteriorly. Many factors account for these differences, most important of which are the histologic grade of malignancy,—the more anterior lesions are usually of lower grade,—the size of the lesion, the mobility of the part, accessibility for treatment and the extent of lymphatic drainage. Recurrence of the primary lesion or the appearance of metastases is rare after three years of freedom from disease,⁴ although the tendency to the formation of multiple new cancers is relatively high.³⁴ Much of the advance in the therapy of lesions of the oral cavity and respiratory tract is due to the splendid work of Coutard,³⁵ who advocated the protracted type of radiation. This principle used elsewhere in the body has also resulted in the eradication of cancers that would

otherwise have been considered hopeless. It has its greatest value in the treatment of inoperable disease, particularly that involving the tonsils, pharynx and larynx.

Lip

The end results in cancer of the lip include only those lesions that arise on the mucous membrane. Those that appear first on the skin of the lips and invade the mucous membrane secondarily may behave like true lip cancers, but in actuality are skin cancers. Reports of five-year cures range from 59 to 70 per cent, but include both absolute and relative figures.³⁶⁻⁴⁵ Subdivision of results into cases with and without lymph-node metastases gives a better idea of the prognosis in the single case. If the nodes are not involved the curability rate is approximately 85 per cent, whereas with nodal metastases it declines to between 30 and 40 per cent. The uniformity of excellent results from the different clinics is striking and encouraging, in spite of the fact that variations exist in the methods of calculation and therapy. In each instance the series is large, so that the type of case coming to the clinic is not of prime importance. It can likewise be pointed out that most cancers of the lip are of a low grade of malignancy and of relatively small size and that metastases occur in from only 15 to 25 per cent of cases⁴⁷ so that most lesions are favorable for cure.

Buccal Mucosa

The lesions of the buccal mucosa comprise those in which the primary site of origin is the inside of the cheek. Extension of disease to adjacent structures greatly influences the prognosis. Lesions that arise in the anterior portion are most favorable for cure. There are relatively few papers on this subject alone, but taken together they represent a sufficient number of cases to be significant. The five-year curability rate ranges from 26 to 31 per cent, and again the uniformity of results is striking.⁴⁵⁻⁴⁸ The curability rates in cases without metastases approaches 50 per cent, whereas in those with nodal involvement it is approximately 25 per cent, provided cure of the primary lesion is accomplished.⁴⁵

Gingivae

Reports on cancers of the gums should include only those lesions that arise from the mucous membrane overlying the upper and lower alveoli. There is relatively early invasion of the adjacent structures, since the ridges are narrow. This characteristic in itself markedly alters the prognosis. In contrast to lesions of the lip and buccal mucosa, there is a considerable disparity in the end results. Much of this is probably due to the definition of the actual site of origin. In some series

only those lesions that are entirely confined to the gingivae are included, whereas in others, regardless of the extent of disease or the site of origin, all lesions involving the gingivae are taken into consideration. When the disease has extended beyond the gums, the site of origin is sometimes difficult to determine.

Curability rates for lesions of the lower gingiva vary from 15 to as high as 60 per cent,^{45,47-52} and for the upper gingiva they range from 33 to 74 per cent.^{45, 51-54} The figures at the lower extreme usually represent absolute cures, whereas the others are relative rates. This does not entirely explain the discrepancies, and it is not likely that the great differences are due to variations in the technic of therapy alone. The discrepancies would be partially rectified by a definitive method of reporting the actual extent and type of disease.

Palate

In the evaluation of results in this type of cancer, lesions of the hard palate should be separated from those of the soft palate. Lesions of the former are usually less malignant and arise in an immobile part where there is a sparsity of lymphatic drainage. As elsewhere, invasion of adjacent structures alters the outlook. In many cases it is difficult to determine the site of origin, but this is of no practical significance, for if the soft palate is invaded, the lesion behaves as though it had arisen there. Few reports concerning the curability of the lesions are available. In studies restricted to epidermoid carcinoma, three-year cures for lesions of the hard palate were 45 per cent and for those of the soft palate were 20 per cent.⁴⁷ The combined figures for epidermoid cancer of the hard and soft palates range from 30 to 38 per cent.^{45, 55} When considered from the standpoint of histologic type, the five-year rate has been reported as 88 per cent for adenocarcinoma and 38 per cent for epidermoid carcinoma by one group,⁵³ and 23 per cent for all types of malignancy by another.⁵⁶

Tongue

Only those cancers that are confined to or arise primarily in the tongue are included. Some authors do not distinguish lesions of the tongue and floor of the mouth, but this is usually satisfactory since there is little difference in their behavior. The position of the primary lesion is important, since lesions of the anterior portions are usually less malignant. The lesions metastasize early, owing in large measure to the relatively high grade of malignancy, the muscular action of the tongue and the abundance of lymphatics. End-result studies from a large number of clinics reveal variations in five-

year cures from 14 to 37 per cent.^{45, 48, 50, 52, 57-60} Most figures, however, are approximately midway between the extremes—that is, 25 per cent. Cures as high as 50 per cent have been obtained for cancers of the anterior third of the tongue, whereas those for the base are as low as 5 per cent.

Floor of Mouth

There are few studies restricted to lesions arising solely in the floor of the mouth. In this group, five-year cures from 18 to 32 per cent have been published,^{45, 48, 50, 67, 68} but as in cancer of the tongue, most figures are an average of the extremes (25 per cent). The same factors that operate in the prognosis of cancer of the tongue should be considered in lesions involving the floor of the mouth.

Tonsils

Lesions of the tonsils are highly malignant and, as is to be expected, the curability rate is low. Frequently the first sign noted by the patient is a swelling in the neck caused by lymph-node involvement. Most observers^{33, 48, 69-72} report the five-year rate to be about 18 per cent, although two clinics^{48, 69} had rates as high as 30 and 32 per cent. The latter figures are well substantiated, and in this instance it is likely that the methods used represent a definite advance in therapy.

Pharynx

The pharynx is anatomically divided into the nasopharynx, the mesopharynx (the oropharynx, which in reality includes the soft palate and the fauces) and the hypopharynx. As in the case of the tonsils, the first sign may be a swelling in the neck.

The curability rates of cancer of the nasopharynx for five years of 30, 25 and 18 per cent have been recorded.^{35, 73, 74} The average five-year survival rate of lesions of the mesopharynx has been reported as 15 per cent.⁷⁵ The results of treatment in cancer of the hypopharynx are extremely poor and range from 6 to 12 per cent^{35, 48, 76, 77}; these figures were confined to lesions that arose primarily in the hypopharynx.

Larynx

Confusion in the evaluation of end results in cancer of the larynx exists because of differences in the definition of the terms "intrinsic" and "extrinsic." True laryngeal lesions are those that arise in the cavity itself and are intrinsic. Subsequent extension to include the aryepiglottic fold, the pyriform fossa or the postericoid region—which are in reality parts of the hypopharynx—makes it difficult in many cases to determine the primary site of origin. When tumors arise outside of the cavity but in juxtaposition, they are really hypopharyngeal cancers, but have been called

extrinsic lesions of the larynx by many observers. Once the lesion extends beyond the laryngeal cavity, it behaves like lesions that arise in the hypopharynx, so that this differentiation is not significant. Intrinsic lesions, which arise in and remain confined to the larynx, are usually operable, whereas those that extend beyond or arise in the hypopharynx are seldom amenable to surgical removal.

In the previous section, cancers arising in the hypopharynx were considered, but the figures presented below refer not only to those lesions that are truly laryngeal but to those that extend outward to involve adjacent structures as well. The curability rate of intrinsic cancer of the larynx is relatively high. In the operable group treated by laryngofissure—obviously very early lesions—the five-year rate averages about 80 per cent.^{52, 78, 79} One group⁸⁰ reports 96 per cent survivals without disease from two to thirteen years. The results of total laryngectomy average about 55 per cent. The results of therapy in the inoperable group are much lower, but considering the extent of disease in many cases the results are encouraging. For example, Coutard⁸¹ reports 27 per cent five-year cures. It must be remembered that the lymphatic drainage of the true larynx is relatively sparse, whereas that of adjacent structures, including the hypopharynx, is exceedingly rich. Thus, regional lymph-node metastases are much less frequent in the former (18 to 35 per cent) than in the latter (56 to 74 per cent).⁴⁵ It is not surprising that differences in prognosis have been observed between intrinsic and extrinsic lesions of the larynx. The smaller size of the former, the barrier exerted by the laryngeal cage to extension of disease and the lower incidence of lymph-node metastasis are the main factors accounting for this.

THYROID GLAND

Cancer of the thyroid gland is frequently discovered after routine thyroidectomy for other reasons. The prognosis in the cases without clinically demonstrable cancer is excellent, whereas those lesions that are suspected or are detected before operation have a much lower curability. The prognosis is also altered by the frequency of blood-vessel invasion, nodal metastases and dispersion to distant organs. As in the case of cancer of the breast, end results for periods longer than five years are desirable. Portmann⁸² reports 27 per cent five-year survivals in 200 consecutive cases, whereas DeQuervain⁸³ found 31 per cent in a group of lesions diagnosed clinically and subjected to radical operation. Pemberton⁸⁴ had 70 per cent five-year cures in a series of cases in which the lesion was found incidentally or was suspected at operation. As emphasized by Lahey et al.⁸⁵ and by Pemberton,⁸⁴ the prognosis also varies considerably with the histologic type and mode of spread.

The curability is most favorable in papillary adenocarcinoma, in which the rate is as high as 80 per cent, as contrasted with diffuse carcinoma, small-cell or giant-cell carcinoma or sarcoma, where the rate is 20 per cent or less. Fortunately, many of the cases belong to the more favorable group, so that the general prognosis is good.

GASTROINTESTINAL TRACT

It is the opinion of most people that cancer of the gastrointestinal tract is a hopeless disease. Early diagnosis is sometimes difficult and seldom made, especially since patients minimize their symptoms and usually do not report for examination until the disease is relatively advanced. This is truer for cancer of the stomach than for lesions of the colon and rectum. In spite of these shortcomings and considering the magnitude of the procedures in operable cases, the end results are excellent. In recent years, the operability rates for all lesions have risen, which augurs well for the future. At the same time, the mortality rate for radical procedures is declining, because of a better acquaintance with technics and preoperative and postoperative management. Variations in the reported results depend to a large extent on the criteria of operability of the various clinics, the operative mortality and the stages of disease comprising the series reported. Some clinics attack only relatively early lesions, whereas others attempt heroic procedures in an effort to cure the disease. At any rate, it is clear that cancer of the gastrointestinal tract in the operable stage is a curable disease.

Stomach

Approximately 50 per cent of all patients with cancer of the stomach are operable, but actually only about a half of these are suitable for radical curative procedures.⁸⁰⁻⁹⁰ In reality many of these are borderline lesions. The five-year curability rate of all cases that enter the hospital is about 5 per cent.^{87, 88} However, the prognosis in resectable lesions is much brighter in spite of operative mortalities ranging from about 15 to 30 per cent.⁸⁶⁻⁹¹ The rates of survival in this group as reported in large series vary from 15 to 30 per cent, although most of the results are between 20 and 25 per cent.⁸⁶⁻⁹⁸ Some of the figures include operative mortality, whereas others pertain only to those patients who survive the operation. If the lymph nodes are not involved, five-year survival rates range from 45 to 62 per cent, but decline to 18 per cent when the nodes are involved and to about 10 per cent when the neighboring organs are invaded.⁸⁶⁻⁸⁹

Colon

The operability rates in cancer of the colon are fairly high, but the criteria vary in the different

clinics. In recent years, it has been reported as being from 55 to 85 per cent, although the higher figures in this range are unusual.⁹⁹⁻¹⁰⁵ The operative mortality ranges from about 12 to slightly over 20 per cent.⁹⁹⁻¹⁰⁵ The higher rates may have been partially due to attempts to cure patients who were not in the best of physical condition or in whom the disease was fairly extensive. Staging of the operation also alters the mortality rate.⁹⁹⁻¹⁰¹ In general the two-stage procedures have a lower mortality. Ochsner and DeBakey¹⁰⁵ collected the statistics from the literature and found that the operability in different clinics varied from 38 to 81 per cent but averaged 59 per cent. In 2991 collected cases the operative mortality was 22 per cent and the curability rate in nearly four thousand reported resections ranged from 41 to 53 per cent. An absolute cure of 29 per cent has been reported by Cattell and Sugarbaker.¹⁰⁴ There is a definite uniformity of five-year survivals in patients whose lesions were subjected to resection. In clinics caring for large numbers of cases, most figures range from 47 to 56 per cent.⁹⁹⁻¹⁰⁹ The site of the lesion is important. Five-year survivals for cancers of the right colon range from 51 to 71 per cent,^{99, 102, 107, 110} for the transverse colon average about 40 per cent,⁹⁹ and for the left colon average about 38 per cent.^{99, 102, 107} The degree of mural penetration and the grade of the tumor must be considered, especially in relation to lymph-node metastases.¹¹¹ In the absence of positive nodes, the five-year rate for all cases is as high as 63 per cent and only declines to approximately 45 per cent when the nodes are involved. Lesions of low-grade malignancy have the highest curability. For example, it has been reported that Grade I lesions without metastases are curable in 69 per cent of operated cases, as contrasted with 37 per cent in Grade IV lesions. If the lymph nodes were invaded, the survival rates were 55 and 15 per cent, respectively.¹⁰³

Rectum

The operability rate of cancer of the rectum has increased and the operative mortality has declined because of the great advance made in operative treatment, largely through the efforts of Miles, Jones, Lahey and others. The operability rate in cancer of the rectum at the present time ranges from 50 to 75 per cent^{100, 101, 104, 112} and the operative mortality varies from 7 to 13 per cent (average 10 per cent).^{100, 101, 104, 112-115} Cattell and Sugarbaker¹⁰⁴ report an absolute curability of 25 per cent, but the five-year rates on resectable cases range from 38 to as high as 73 per cent.^{100-104, 108, 112-117} The latter figure is unique and is based on a selected group of patients. Most figures approximate 45 per cent.

URINARY TRACT

The two commonest sites of cancer in the urinary tract are the bladder and the kidney. Lesions of the urethra and ureter are relatively rare. Therefore, only the former lesions will be considered.

Bladder

There are a variety of forms of cancer of the bladder, and although many are slowly growing, in general the disease is very lethal. Here as elsewhere, the curability depends on the type and extent of the disease, the grade of malignancy and the degree of radiosensitivity and operability. The method of therapy varies from electrocoagulation or radium implantation for the smaller lesions to partial or complete cystectomy for operable cancer, and to x-ray therapy only for the more advanced cases. The American Urological Association has established a registry for bladder cancer as an aid to better diagnosis and treatment. Ferguson et al.¹¹⁸ analyzed the reports on 658 cases sent into the registry and found that five years following operation 23 per cent were living, but that only 16 per cent were free of disease. Since these were operable lesions, the group must be considered as those favorable for cure. Reports from single clinics usually deal with the results of treatment by different methods or according to the type of lesion. Obviously this represents selection of cases, so that it is difficult to evaluate the actual prognosis of bladder cancer as a whole.

In lesions amenable to local radium implantation, the recent five-year cure rates vary from 38 to 44 per cent.¹¹⁹⁻¹²¹ Only 10 per cent of the more advanced cases, treated by x-ray alone, survive without disease five years after treatment.¹²² Five-year cures of infiltrating cancers of the bladder are as high as 55 per cent if treated by total cystectomy, but are only 18 per cent when partial cystectomy is done.¹²³ Barringer,¹²⁴ in a comprehensive study of 257 patients undergoing all types of therapy, found a 40 per cent five-year relative rate (based on 211 cases) and an absolute rate of 33 per cent. If the lesion was of papillary character, the relative cure was 56 and the absolute cure 45 per cent; if infiltrating, it was 29 and 25 per cent, respectively.

Kidney

There are few recent reports on cancer of the kidney, and these have to do with favorable lesions. Smith¹²⁵ combined various reports and quotes a five-year survival rate of 19 per cent. The figures of Hyman¹²⁶ and of Beer¹²⁷ are almost identical. They found an operative mortality of about 10 per cent and a curability rate of 33 per cent of the survivors. Priestley¹²⁸ reported that 38 per cent of patients with hypernephroma, 35 per cent of

those with epidermoid cancer of the renal pelvis and 20 per cent of those with Wilm's tumor (adenofibrosarcoma) survived for five years following operation.

MALE GENITAL TRACT

Cancers of the male genital tract, except those involving the penis, have a low curability rate, especially since few patients present themselves for treatment in the early stages. Furthermore, cancers of the testicle and scrotum are usually highly malignant, whereas cancer of the prostate, although usually quite slowly growing, seldom causes symptoms until the disease is fairly well advanced. Since cancer of the scrotum is fairly rare, it will not be discussed.

Penis

Cancer of the penis behaves like that of the lip regarding its mode of growth, grade of malignancy and propensity to metastasize. Many patients, however, report for treatment when the disease is advanced, so that the chances for cure are less favorable. The usual five-year curability rates range between 33 and 50 per cent^{15, 129-132}; in highly selected and favorable cases they are as high as 75 per cent.¹³³ The rate is about 60 per cent in the cases without lymph-node involvement and declines to 25 per cent when lymph nodes are invaded. If cure of the local lesion is obtained in the latter group, the curability rises to 42 per cent.¹⁵

Testicle

Cancers of the testicle except for the teratomas are usually highly malignant and metastasize early to the regional, periaortic and thoracic nodes as well as to distant organs. Chorioepitheliomas are the most malignant, and cures are seldom recorded. Dean¹³⁴ found 29 per cent of five-year cures in 170 cases of all types of testicular tumor. In 23 without demonstrable metastases, however, the rate was 79 per cent. Smith et al.¹³⁵ reported 15 per cent of their patients as alive and well two years or more after treatment. Higgins and Buchert¹³⁶ state that five years is not a long enough follow-up period to establish the final result and report 14 per cent ten-year cures. Leddy and Desjardins¹³⁷ report 53 per cent five-year survivals in obviously selected cases, and state that in cases without metastases at the time of treatment there is a 60 per cent chance of surviving five years or longer, whereas other cases have a 30 per cent probability. Payne¹³⁸ found 40 per cent of 38 cases free of disease for five years.

Prostate

Until the advent of castration and the use of estrogenic hormones in the treatment of cancer of the prostate, the curability rate was exceedingly

low.¹³⁰ A considerable time must elapse to evaluate the efficacy of this new treatment, but there is no question that as a palliative, even if not a curative, measure it greatly increases the life expectancy of men suffering from this disease. It is unusual to detect the lesion in its early stages, and many are found only after prostatectomy for clinically benign hypertrophy. Barringer's¹⁴⁰ figures from an unselected group of cases demonstrate strikingly the stage of disease when his patients were first seen. Less than 5 per cent of the tumors were small, 7 per cent were medium, and 88 per cent were classed as large. The series included 351 patients, of whom only 8 per cent of 322 followed were living and well for three to seventeen years. Smith¹⁴¹ reported 28 per cent living from one to five years or more in early and moderately advanced cases treated by total perineal prostatectomy. In early cases selected and treated by the same operation, the following percentages of five-year cures have been recorded: Belt,¹⁴² 58 per cent; Young,¹⁴³ 53 per cent; and Colston,¹⁴⁴ 50 per cent.

FEMALE GENITAL TRACT

Comprehensive reports of the results of many clinics in cancer of the female genital tract have been published by Meigs¹⁴⁵ and by Morton.¹⁴⁶ Consequently, the reader is referred to these publications for details. The lesions differ considerably in histologic type, in radiosensitivity and in accessibility for treatment by radiation or surgery. Hence, treatment for each lesion is governed by these considerations. Only the commoner lesions are discussed below.

Vulva

Cancer of the vulva usually occurs in the older age groups and is usually of squamous-cell origin. These lesions as a rule do badly with radiation, so that they are essentially a surgical problem. The lesions frequently grow rapidly, metastasize freely and early to the regional lymph nodes, and have a great tendency to develop local recurrence. The development of new primary cancers in the same region after previous vulvectomy is not unusual. Representative five-year cure rates vary from 26 to 32 per cent.¹⁴⁷⁻¹⁵⁰ All authors agree that the early lesions yield a high percentage of cures, but there is a considerable decline when the nodes are involved.

Vagina

Reports on the cure of cancer of the vagina are scarce. In general the curability rate is quoted as 30 per cent.¹⁵¹

Cervix

Cancer of the cervix is the commonest form of cancer of the female genital tract and is usually

of squamous-cell origin. It spreads early to adjacent structures, such as the vagina, broad ligaments and uterine cavity; in addition, it metastasizes freely to the regional lymph nodes. A number of classifications have been proposed to facilitate evaluation of the end results. This is essential because of the marked differences in the stage of the disease when the patient is first seen. Except for minor variations all are in essential agreement. The stages are roughly classified as:

Stage I. Confinement of disease to the cervix.

Stage II. Involvement of the vagina or extension into the uterine cavity.

Stage III. Extension to one or both broad ligaments.

Stage IV. Fixation of the uterus, or wide extension into both broad ligaments or into the bladder or rectum, or distant metastases.

The literature on cancer of the cervix is voluminous. Since the lesions are usually radiosensitive, there are a large number of papers dealing with the relative merits of operative versus radiation procedures in the treatment of the more favorable cases (Stages I and II). The reports from most clinics, however, reveal that the greatest number of cases are first seen in the more advanced stages. The majority of reports of five-year end results for all stages combined vary from 20 to 40 per cent.¹⁵²⁻¹⁷⁵ These differences are partially accounted for by the method of reporting and by the percentage of each stage in any one clinic. The average report reveals figures midway between the extremes. Five-year cures by stages are as follows, the lowest figures usually representing absolute cures: Stage I, 40 to 80 per cent; Stage II, 34 to 65 per cent; Stage III, 13 to 35 per cent; and Stage IV, 0 to 8 per cent.

Although radiation is used almost entirely in some clinics, there are many advocates of radical hysterectomy (Wertheim, abdominal route, or Schauta, vaginal route) for the earlier cases. One of the major indications is the removal of lymph-node metastases, which ordinarily are not only resistant but also inaccessible for adequate irradiation. So far as the local lesion is concerned, either radiation or surgery is an efficient method of therapy. Occasionally an early lesion is radioresistant, and in these cases surgical removal can usually be done subsequently. Bonney,¹⁵⁴ who advocates Wertheim hysterectomy, found an operability rate of 63 per cent and reports five-year cures of 40 per cent; in cases without nodal involvement the curability rate was 53 per cent, and in those with nodal metastases, 22 per cent. This is to be compared with the results of radiation, especially since the mortality is higher from operation (average 15 per cent) than from radiation (usually less than 3 per cent), even in the most skilled hands. There-

fore, this must be balanced in judging the efficacy of any therapy. Nevertheless, it is apparent that no one form of therapy suffices for all cases, and as in cancer elsewhere, the decision concerning the merit of any treatment should be made in the given case.

Fundus of Uterus

Cancers of the endometrium are usually adenocarcinoma and differ considerably in their radiosensitivity. The lesions may remain confined to the uterine cavity for a long period of time before they penetrate the myometrium or spread to the cervix. Metastases to lymph nodes occur relatively late in the disease. The usual treatment of the operable lesions at the present time is total hysterectomy. The inaccessibility of the lesion for local radiation therapy, the difficulty in determining the exact site of origin and the frequent radioresistance of the lesions favor the employment of surgical procedures wherever possible. However, cures in operable cases may be obtained by judicious radiation therapy. Many clinics now combine the methods by inserting radium into the uterine cavity and subsequently performing a hysterectomy.

The curability for operable cancer of the endometrium treated by hysterectomy alone or combined with radiation is high; that of the inoperable group is quite low. Statistics do not as yet prove the value of complementary radiation in surgically treated cases. Five-year survival rates, including therapy of all types in all cases, average about 40 per cent (range 35 to 45 per cent).^{157, 161, 167 170-183} Hysterectomy alone or in combination with radiation yields cures of 48 to 70 per cent in the operable group, whereas radiation alone—including both operable and inoperable cases—produces relative cures of 35 to 45 per cent. The published figures comparing the relative merit of surgery and radiation in operable cases favor the former, but this is to be expected, since the operative mortality is low (2 to 4 per cent) and eradication of the disease is more certain. Nevertheless, in poor-risk patients and in the inoperable group, radiation can be expected to give good results.

Ovary

There are a number of histologic types of cancer of the ovary. Difficulties in the classification of these tumors exist because of variations among the forms. The rate and mode of growth are of particular importance in the curability of the lesions. Encapsulated tumors offer the greatest chance for cure. When the cancer has spread beyond the ovary and cure cannot be attained, the survival rate with disease present may still be considerable, since many of the lesions are slowly growing. Fur-

thermore, some of the tumors are radiosensitive, so that the life expectancy without cure may be further increased by radiation. Unfortunately, the tumors seldom produce symptoms until the process is fairly well advanced, so that the over-all curability rate is not so high as one would hope.

Meigs¹⁸⁶ reports a 16 per cent 5-year survival rate. This figure is absolute regarding the prognosis of all types of ovarian cancer after treatment. Early cases have a higher curability rate. Lynch¹⁸⁷ points out that because of the individual characteristics of growth, the five-year period is inadequate for evaluation of cure. Recurrence of slowly growing tumors may not be detected before this interval, thus making estimation of clinical cure difficult. His figures reveal a 35 per cent five-year survival rate following treatment. Walter et al.¹⁸⁸ discuss the merits of radiation in conjunction with surgery. Their five-year results for treatment with surgery alone were 6 per cent, with surgery and inadequate radiation 10 per cent, and with adequate radiation 29 per cent. These figures are difficult to assess, since the terms "inadequate" and "adequate" are matters of definition.

SARCOMAS

In general, the curability of sarcomas is low, except when the disease is treated in the early stages. Even then control of these lesions is difficult because of the great tendency to metastasize through the blood stream.

Malignant Melanoma

Malignant melanoma metastasizes freely by way of either the lymphatics or the blood stream. It is radiosensitive in about 10 per cent of cases. The criteria of malignancy used by the pathologist are of major importance in the end-result reports. Five-year curability rates vary from 22 to 42 per cent.^{45, 189-192} As in other reported series, most of the figures are midway between these extremes.

Fibrosarcoma

Fibrosarcoma rarely metastasizes through the lymphatics, but it is difficult to eradicate locally and spreads freely through the blood stream. Three-year cures average about 21 per cent, whereas the five-year rate is approximately 18 per cent.¹⁰¹⁻¹⁹⁰

Osteogenic Sarcoma

The American College of Surgeons has established a registry for bone tumors for the purpose of verifying the diagnosis, for evaluating the various forms of treatment, and for a better understanding of the course of the disease. There is a wide variation in the histologic type and in the site of origin. The accessibility for treatment and the frequent blood-stream metastases influence the

prognosis. Reports reveal five-year survival rates in favorable cases of 19 to 39 per cent (average 30 per cent).¹⁹⁷⁻²⁰² The higher results refer to those most suitable for operative treatment. The results in all cases are obviously lower, but the figures are of importance as indicating that treatment of the disease is not hopeless.

Malignant Lymphoma and Hodgkin's Disease

The lesions of malignant lymphoma and Hodgkin's disease are usually highly malignant and very radiosensitive. As a result, even though the eventual curability rate is exceedingly low, the prolongation of life by radiation is considerable. Variability in histologic type and the mode of spread of the individual forms frequently alter the prognosis.^{203, 204} Several reports reveal that in certain types of the diseases a number of patients survive for five years and that in some cases the disease has been completely controlled.²⁰³⁻²⁰⁶

OTHER ORGANS

It is too early to appraise the results of the newer concepts of treatment of such cancers as those of the esophagus, lungs, duodenum, bile ducts and pancreas. Formerly these lesions were considered as hopeless, but as previously pointed out,¹ the recent rapid strides in surgical treatment offer hope of a cure of a reasonable number of patients.

* * *

The present-day treatment of cancer is effective in controlling the disease in its various manifestations. In several forms the rate of cure is even higher than that of some other diseases. It cannot be emphasized too strongly, nor be repeated too often, that the prevention, early diagnosis and treatment of cancer are the means to a better curability rate. Palliative therapy for the more advanced lesions is of great value in the prolongation of life and in the alleviation of suffering in the final stages of the disease.

Variations in the methods of reporting end results make it difficult to gauge accurately the curability rates in the different types of cancer. Nevertheless, even at present, it is clear from a careful analysis of the statistics of clinics throughout the world that there is a fairly good agreement in the survival rates. It is hoped that more uniform and complete methods of reporting results will be adopted, so that series of cases from each clinic can be compared directly, which may lead to more efficient therapy.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**BENJAMIN CASTLEMAN, M.D., *Acting Editor*EDITH E. PARRIS, *Assistant Editor*

CASE 29371

PRESENTATION OF CASE

A thirty-two-year-old housewife was admitted to the hospital because of stupor and convulsions of eighteen hours' duration.

For the past ten years the patient had had bronchial asthma, for which she had been repeatedly admitted to this hospital. No definite causative agent could be identified, but she was known to be sensitive to morphine, codein, aspirin and barbiturates, and she had been taught to give herself adrenalin subcutaneously and aminophyllin intravenously. During her fifth admission, five and a half years prior to the present one, she had had an attack of violent abdominal pain associated with diarrhea. At that time the spleen was found to be "easily palpable." The abdominal pain cleared up without residual, and during the next eight months, when she had been examined repeatedly in the Out Patient Department, the spleen had not been felt. The sixth hospital admission had been occasioned by a miscarriage at three months, from which she recovered uneventfully. The seventh admission was about four and a half years before the final one, because of marked increase in the severity of her asthma associated with the production of blood-tinged sputum. There were signs of consolidation at the left base and culture of the sputum grew Type 1 pneumococcus. She recovered uneventfully without the aid of serum or chemotherapy. At that time the spleen was again palpated and the liver edge was felt 2 cm. below the costal margin. After discharge she continued to have asthma but was able to control her symptoms by means of adrenalin and aminophyllin. Four months before her final entry to this hospital she was admitted to another hospital, where an acutely inflamed appendix was removed. At the same operation a uterine dilatation and curettage, a bilateral salpingectomy and a left oophorectomy were performed. Following the operation the patient was well, except for profuse vaginal discharge, until three days before entry, when she felt as if she had the "grippe." She became so cold and chilly that she had to use hot water bottles and extra blankets. There was a feeling

of "feverishness in the inside." She lost her appetite and developed headache, pain in the back of the neck and pain across the lumbar region of the back. One day before admission she became confused and irrational. Although her asthma had decreased markedly during the day or two preceding entry, seven empty aminophyllin ampules were found near the bed the night before admission. About 2:00 a.m. of the day of admission she became rigid and opisthotonic, and then "shook all over" and frothed slightly at the mouth. The attack lasted about five minutes, during which time she was completely unconscious. Her physician, who arrived forty-five minutes later, gave her 1 cat unit of digitalis intramuscularly to "slow the heart, which was beating 130 to 140 per minute." Later that day she became more stuporous and irrational. A second physician was called, who sent her to the hospital.

Physical examination showed a well-developed and well-nourished woman breathing in a rapid and labored fashion. She was somewhat lethargic and would not answer questions except with "yes" and "no." The tongue was moderately dry. There was moderate resistance to flexion of the neck, and she was unable to place her chin on the chest. The lungs were resonant, and the breath sounds coarse and rough throughout, with a few wheezes. There was generalized tenderness to deep palpation of the abdomen, and bilateral costovertebral angle tenderness. An irregular ecchymotic area was present on the radial aspect of the right index finger. The biceps, triceps, radial, knee and ankle jerks were equal and active. The Babinski, Chaddock, Gordon and Oppenheim tests were positive on the left, with unsustained ankle clonus and a doubtful Kernig sign; all were equivocal on the right.

The red-cell count was 3,580,000, with a hemoglobin of 11 gm. The white-cell count was 13,200, with 80 per cent neutrophils; on smear, there was marked shift to the left, and toxic granulation of the neutrophils. The urine was acid with a + test for albumin and for acetone; the sediment contained 5 to 6 white cells per high-power field and innumerable red cells and granular and cellular casts. Lumbar puncture gave an initial pressure of 165 mm. and a final pressure of 120 mm. after 10 cc. of fluid had been withdrawn. The spinal fluid was faintly cloudy and contained 20 polymorphonuclears, 50 lymphocytes and 830 fresh red cells per cubic millimeter; many intracellular and extracellular gram-negative biscuit-shaped diplococci were seen in the smear, but culture on various mediums gave no growth. Spinal-fluid Wassermann and Hinton tests were negative; the protein was 33 mg., and the sugar 53 mg. per 100 cc. A blood culture taken on the

*On leave of absence.

day of admission was reported positive for *Staphylococcus aureus* (coagulase positive) in both flasks. A blood Hinton test was negative.

Half an hour after admission the patient was given 5 gm. of sodium sulfadiazine in 500 cc. of saline intravenously. The following day the neck was less stiff, the headache was less and she was more responsive although still quite restless. Respirations were labored, and the lungs were full of rhonchi and wheezes. She was given intravenous fluids and 2 ampules of aminophyllin without much apparent improvement. The sulfadiazine level on that day was 13 mg. per 100 cc.; the non-protein nitrogen, 37 mg. per 100 cc.; the chloride, 88.3 milliequiv. per liter; the carbon dioxide combining power, 20.1 millimols per liter; the protein, 6.5 gm. per 100 cc.

On the second hospital day, three successive white-cell counts were 4700, 3800 and 3700 respectively, with 93 per cent toxic-appearing neutrophils. The sulfadiazine was stopped. The following day the temperature was 100.4°F, and the white-cell count 3500. An x-ray film of the chest, taken with a portable machine on the fourth day, showed mottled increased density at the right base that seemed to be less than it was at the time of examination a year previously. The lung markings were prominent throughout the chest, which was quite emphysematous. The right costophrenic angle was obliterated. No evidence of abscess or bronchiectasis could be demonstrated.

The temperature on the following day rose to 104.4°F. The patient complained of severe headache and pain in the left shoulder and right hip. The ecchymotic area on the right forefinger had broken down, with discharge of reddish-brown purulent material. Similar bluish-black ecchymotic areas were found on the tip of the fifth finger, the sole of the left foot and the right heel. A large area of swelling, exquisite tenderness and redness appeared on the right buttock, near the site of an intramuscular injection of paraldehyde, from which colon bacilli, hemolytic *Staph. aureus* (coagulase positive) and alpha-hemolytic streptococci were cultured subsequently. There was a profuse, greenish, creamy, vaginal discharge, in which many gram-positive cocci in small clumps were seen on the smear. A lumbar puncture gave a clear fluid containing 29 red cells, 2 polymorphonuclear cells and 5 lymphocytes per cubic millimeter. The initial pressure was 275 mm.; the final pressure, 100 mm. The spinal-fluid protein was 31 mg. per 100 cc., and the sugar 64 mg.; culture again yielded no growth. The temperature remained between 102 and 104.5°F. Two other blood cultures were reported positive for hemolytic *Staph. aureus* (coagulase positive). The

white-cell count rose to 10,600 on the sixth hospital day.

The patient received 4 gm. of sulfadiazine on the seventh and eighth hospital days and then continued on daily doses of 6 gm. of sulfathiazole. She complained of severe pain in the left anterior chest, where a loud grating pleuritic friction rub could be heard. There was no cough or hemoptysis. The white-cell count was 11,500; the urine showed a ++ test for albumin and contained numerous white and red cells.

On the ninth day many petechiae were noted on the flexor surfaces of the hands and feet, on the conjunctivas and in the buccal mucosa. On the eleventh hospital day the patient's condition was essentially the same. The sulfathiazole level was 13.4 mg. per 100 cc., and the nonprotein nitrogen 52 mg. The blood culture was still positive for hemolytic *Staph. aureus* (coagulase positive). The white-cell count was 12,300. The temperature ranged between 101 and 104°F. The urine showed a ++ test for albumin and a ++++ test for diazine crystals.

On the twelfth day the patient had a convulsion. The sulfathiazole level was 15.2 mg., and the nonprotein nitrogen 120 mg. per 100 cc. The carbon dioxide combining power was 23.2 millimols, and the chloride 74.5 milliequiv. per liter. The white-cell count was 13,500, and the hemoglobin 9 gm. per 100 cc. The spleen was felt for the first time since admission. The sulfathiazole was stopped, and the patient was given 20,000 units of penicillin intravenously, followed by two similar doses in the next four hours and then 10,000 units every two hours for the next two days. Her condition remained about the same. On the fifteenth day she had repeated convulsions and became comatose. The sputum was bloody. There was considerable breakdown of the tissue over the back, the buttocks and the right heel.

An x-ray film of the chest showed a few small linear areas of increased density just behind and above the left diaphragm. No frank areas of consolidation or evidence of pleural effusion or empyema could be seen. A lumbar puncture revealed an initial pressure of 85 mm. The fluid contained 600 red cells, 130 polymorphonuclear cells and 6 lymphocytes per cubic millimeter; no microorganisms were seen in the smear. The blood culture was still positive. The patient received three transfusions of 500 cc. of blood in the following three days and considerable intravenous fluid. The urinary output, however, became very low, and she developed diarrhea. The temperature ranged between 103 and 105°F., the pulse above 100, and the respirations about 40; the blood pressure was 70 systolic, 10 diastolic. The white-

cell count was 17,000, with 84 per cent neutrophils. Injections of 25 per cent glucose in saline were given intravenously, with no apparent effect on the output of urine.

On the nineteenth hospital day the patient's condition appeared worse. She developed anasarca. The left arm was slightly stiff; the left biceps and triceps reflexes were present, but no other reflexes could be elicited. The temperature was 104°F. She was given 40,000 units of penicillin every two hours for five doses without any apparent benefit, and died on the twentieth hospital day.

DIFFERENTIAL DIAGNOSIS

DR JOHN NORCROSS*: I think it is fair to say that it is not easily possible to connect all the conditions in this case under one diagnosis. I am going to say that the first part of the story is not connected with the second; that is, the long history of asthma and the violent abdominal pain and palpable spleen recorded at one admission are not related to the events that occurred in the last admission. What caused the abdominal episode, I do not know. We are not given much detail about it and I do not believe, from the point of view of the final episode, that it is important. Four and a half years previously she had had pneumonia, and at that time the spleen was again palpable. I assume from the history that it was then no longer palpable until the final admission.

I think we might date the present illness from four months before the final entry. She continued to have asthma, but at that time she was taken to another hospital where an acutely inflamed appendix was removed. At the same time a uterine dilatation and curettage was done and some of the pelvic organs removed. I think we can safely say that she had a profuse vaginal discharge shortly after this operation, and probably before it also, and since her tubes and one ovary were removed, she may well have had chronic pelvic inflammatory disease, for which this operation really was done. Regarding the appendix, it may or may not have been acutely inflamed.

Two days before entry the patient became acutely ill with fever, chills and rapidly developing signs of meningismus and meningitis. We are told that seven empty ampules of aminophyllin were found near the bed. I have never seen a patient who received the contents of seven aminophyllin ampules in a short course of time; that might cause a convulsion, but I doubt it. In any case I do not believe that it is important from the point of view of the final diagnosis.

At the time of entry to the hospital she was found to be stuporous and had signs that were

consistent with meningeal irritation. She also had an ecchymotic area on the right index finger, and positive Babinski and related signs on one side, which are perhaps unusual at this time in the course of meningitis but not at all impossible. She had some degree of anemia, a slight leukocytosis and, what is more important, a marked shift to the left, with toxic granulations in the polymorphonuclear leukocytes.

The urine was abnormal but we do not know whether it was a catheterized specimen. Since she had a profuse vaginal discharge, some of the white cells may have come from the vagina, but the changes were primarily due to disease of the urinary tract. The cellular findings and the granular and cellular casts all signify serious irritation of the kidneys.

The lumbar puncture gave an initial spinal fluid pressure of 165 mm., and a final pressure of 120 mm. I wonder if the initial pressure could have been higher. The fluid was faintly cloudy, and the cell count showed only a few polymorphonuclear cells, 50 lymphocytes and 820 fresh red cells. Regarding the red cells, I should like to know whether they were present in the early part or at the end of the tap; they may have been the result of difficulty in tapping. "Many intracellular and extracellular gram-negative biscuit-shaped diplococci were seen in the smear." That is the most important finding. They could have been one of two organisms,—gonococci or meningococci,—and I think at this point we should decide which was the more likely. Apparently the service never knew because they were unable to grow them out on a culture medium. The sugar was 53 mg per 100 cc., which is certainly high for an acute meningitis. A blood culture taken at the same time was reported positive for *Staph. aureus* (coagulase positive). This was repeated several times throughout the rest of the course in the hospital, and we know, therefore, that the patient had a true bacteremia due to a pathogenic staphylococcus. We also know that four months previously the patient had had a radical pelvic operation, presumably associated with an infection in the pelvis, which was likely caused by the gonococcus. Therefore, I am going to venture the guess that this was a gonococcal meningitis.

The patient was given sulfadiazine and responded quite satisfactorily, but they apparently dared not give more because the white cell count rapidly dropped either because of the toxicity of the condition or because of sensitivity to the drug. We learn later that the clinical symptoms improved and that a second tap done shortly thereafter was negative. No organisms were seen in the smear, and the culture yielded no growth.

*Physician, Lohrey Clinic.

The patient then began to take a definite turn for the worse and there were other manifestations, first in the joints, then in the skin and then subcutaneous abscesses. We can therefore say that she had a definite bacteremia, and we have adequate proof from the blood cultures that a pathogenic staphylococcus was the etiologic organism. She then developed pleuritis, further skin manifestations, with petechiae, and additional evidence pointing to trouble with the kidneys. We are told that she had many sulfadiazine crystals in the urine. We also know that at that time the sulfadiazine was changed to sulfathiazole. We wonder, of course, what role these drugs played in the kidney picture. I think we can assume that they played some part, but a minor one. There was evidence of nephritis as the story started, and I think that the later picture was largely a progression of that condition. On the twelfth day she had a convulsion. At that time the nonprotein nitrogen was 120 mg. A lumbar puncture was done shortly thereafter, at which time the spinal fluid contained red cells, polymorphonuclear cells and lymphocytes, but no microorganisms. The blood cultures were still positive. The convulsion might have been caused by the uremia, but I think that it was mostly due to infiltration of the central nervous system by the infection. The urinary output became low, she developed diarrhea and further evidence of uremia, and in spite of the fact that penicillin was given, she rapidly grew weaker and died.

In summary, we have a patient with a picture suggesting gonococcal meningitis, from which she apparently recovered. She then developed evidence of a severe bacteremia, with multiple embolic phenomena of a septic type. There are several possible sources for the bacteremia. The pelvis was the obvious source, and at one point the vaginal smear showed a pathogenic organism that was morphologically identical to that found in the blood culture. I assume that this was the primary source of the organism. The patient also had subcutaneous abscesses, which might have been the source of the bacteremia, but I think that they were secondary rather than primary. The causative organism—a staphylococcus—should have responded better than it did to the sulfonamide drugs, and most certainly to penicillin, unless it was in a place that was difficult to reach, such as the heart valves. The heart is not mentioned in the entire history, and I assume that the physical findings were negative. Nevertheless, that is often true in acute bacterial endocarditis, and it seems to me that the most likely diagnosis is, in addition

to the gonococcal meningitis, an acute bacterial endocarditis, due to *Staph. aureus*, the original source having been in the pelvis. We know that the patient had bronchial asthma and that she had bacteremia and, terminally, septicemia. I think she also had embolic glomerulonephritis, with sulfadiazine contributing to the kidney failure and uremia. She may have had multiple brain abscesses or one abscess as part of the general process.

DR. WILLIAM BECKMAN: On the ward we were as bewildered as Dr. Norcross was by the presence of gram-negative intracellular organisms in the spinal fluid obtained at first lumbar puncture, but in view of the prevalence of meningitis at that time we assumed that they were meningococci. When the patient did not respond to chemotherapy we abandoned that idea. We were considerably less astute on the ward than Dr. Norcross because we did not combine the previous abdominal operation with the present illness.

DR. FRANCIS M. RACKEMANN: This woman had been a patient in the Allergy Clinic for some years. The interesting thing was the method by which she relieved her attacks. She took aminophyllin intravenously two or more times every day for months at a time, and had been giving it to herself. Her husband also learned how to administer it. When I was asked to see her, my first thought was that she was responsible for the septicemia, because she often told me that she carried her syringe loose and "naked" in her handbag along with her handkerchief and other things and that if she was caught with an attack when she was downtown on a shopping tour she did not bother to wash or clean it in any way, but used it as it was to give herself an intravenous injection. I should like to add that, as is so often the case, the asthma, which was so severe and so persistent, having occurred daily for some years, cleared entirely during the infectious period.

CLINICAL DIAGNOSES

Septicemia (*Staph. aureus*).
Acute bacterial endocarditis (*Staph. aureus*).

DR. NORCROSS'S DIAGNOSES

Acute bacterial endocarditis (*Staph. aureus*).
Bacteremia and septicemia (*Staph. aureus*).
Embolic glomerulonephritis.
Uremia.
Brain abscesses?
Gonococcal meningitis, healed.
Bronchial asthma.

ANATOMICAL DIAGNOSES

Pelvic abscess, with extension to right buttock.

Septicemia (*Staph. aureus*).

Acute bacterial endocarditis, mitral valve (*Staph. aureus*).

Septic infarcts of brain, meninges, lung, kidney and spleen.

Subcutaneous abscesses.

(Bronchial asthma.)

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Of course, the most interesting feature of this case was to discover the source of the obvious staphylococcal septicemia. We found a bacterial endocarditis on the mitral valve—a large, friable, shaggy vegetation, 2 by 2 by 1 cm., attached to one of the leaflets, without any underlying old disease of the valve. This indicates that the lesion was acute rather than subacute, the latter usually developing on a previously damaged valve. On microscopic examination the vegetation was filled with staphylococci.

There was a very large abscess in the right pelvis; it was intraperitoneal and extended down to the obturator foramen, connecting with a large sloughing ulcerating infection on the right buttock. Both tubes had been partially removed. The ovaries were still present and did not appear to be infected. The fundus of the uterus contained a great deal of friable material, and this proved to be inflammatory. Since there was no extension through the wall of the uterus, I do not believe that the uterus was the primary source. I am still not sure whether the abscess was the residuum of an acute appendicitis or of acute pelvic inflammatory disease, and I do not know how one can tell. The abscess was tremendous. The fact that it was on the right rather than bilateral is a bit in favor of its having been due to appendicitis. The organism was the staphylococcus rather than the colon bacillus, which is the usual finding in abscesses following appendicitis, but during the long period following operation the staphylococcus might have overgrown the colon bacillus. There were subcutaneous abscesses throughout the body. The spleen weighed 1030 gm. and contained numerous septic infarcts, which had broken down and formed abscesses. A few small infarcts were present in the kidneys, and numerous abscesses of all ages were found in the lung. There was no embolic glomerulonephritis, and no evidence of sulfonamide changes in the kidneys.

Dr. Kubik will tell us about the brain.

DR. CHARLES S. KUBIK: The brain showed numerous septic infarcts and several small abscesses, one of which was about 1.5 cm. in diameter. I should like to ask about the biscuit-shaped organisms found in the spinal fluid.

DR. BECKMAN: The fluid was examined by several extremely reliable people; but, of course, it is possible that they were overdecolorized staphylococci.

DR. KUBIK: I should say that the meningeal symptoms were almost surely related to the bacterial endocarditis. There were patches of subarachnoid exudate, such as are frequently observed in subacute or acute bacterial endocarditis; these usually result from septic emboli to meningeal vessels rather than from septic infarcts within the brain substance.

CASE 29372

PRESENTATION OF CASE

First admission. A fifty-one-year-old housewife was admitted to the hospital because of swelling of the abdomen and jaundice of several weeks' duration.

Twenty-eight months before admission, she developed "grippe," with fever of 104°F., weakness, anorexia and malaise. The abdomen was enlarged. There were jaundice and right epigastric pain. She was admitted to a community hospital where, following x-ray examinations, she was told that she had three tumors but that she was too weak to be operated on. She was discharged home under the care of a practical nurse. During the next seven months she was bedridden, and although she lost 15 pounds of weight, she gradually gained strength and resumed her household activity for the next eighteen months. The jaundice had apparently disappeared. At that time, that is, three months before admission, she fell, striking the chest and right side of the abdomen. Five days later she had a swelling of the right knee, which persisted for several days. The vague pain in the right upper quadrant returned. One month before entry she developed a "cold" and coincidentally became jaundiced. The urine became dark, but no change in the character or color of the stools was noted. Three weeks before admission her abdomen and feet began to swell and steadily became larger. During one week she had nocturia (three or four times). Her appetite had been poor for the three weeks preceding entry, but there had been no nausea or vomiting.

Five years before admission, following her husband's death, the patient began drinking hard liquor—mostly gin—rather heavily and "stopped eating."

Physical examination showed deep jaundice of the skin and scleras. Numerous telangiectases were present on the face and neck, and there were many dilated superficial veins over the abdomen. A few dry râles were heard at the right base. The abdomen was large and tense, and the umbilicus

was everted. There was a definite fluid wave, with bulging flanks. The liver was easily ballotable 11 cm. below the costal margin in the midclavicular line; the edge was vaguely irregular and could also be felt on the left side of the abdomen. The spleen was palpable 4 cm. below the left costal margin. There was moderate pitting edema of the feet and lower legs. The ankle and knee jerks were absent.

The blood pressure was 140 systolic, 80 diastolic. The temperature was 99.3°F., the pulse 104, and the respirations 19.

The urine was brown, had a specific gravity of 1.018 and gave a +++ test for bile. Examination of the blood showed a red-cell count of 3,250,000, with a hemoglobin of 70 per cent. The white-cell count was 14,900, with 62 per cent neutrophils. The stools were brown, mushy and guaiac negative. The blood protein was 8.9 gm. per 100 cc., the albumin being 3.4 gm. and the globulin 5.5 gm., making an albumin-globulin ratio of 0.6; the van den Bergh test was 13.1 mg. direct and 19.6 mg. indirect. The prothrombin time was 38 seconds (normal, 18 seconds). The hematocrit was 40. A blood Hinton test was negative.

On the second hospital day a paracentesis yielded 5000 cc. of clear bile-colored fluid with a total protein of 1.7 gm. per 100 cc. No sediment could be obtained. Culture gave no growth. Palpation of the abdomen then revealed a firm, nodular, irregular, tender liver extending across the upper abdomen down to 3 cm. above the umbilicus. The spleen was palpable four fingerbreadths below the costal margin. The patient was placed on a high-vitamin, high-carbohydrate diet. X-ray examination on the sixth hospital day showed a high diaphragm on both sides, a small amount of fluid in both pleural cavities and a transverse position of the heart.

The patient was now given 1 ampule of Hykinone daily. During the first ten days she was weak, drowsy and nauseated. The pulse was elevated. Later, however, her general condition improved appreciably. On the fifteenth hospital day the temperature and respirations were about normal, and the pulse 90 to 100. The blood protein was 5.6 gm. per 100 cc., the albumin being 3.4 gm. and the globulin 2.2 gm., making an albumin-globulin ratio of 1.6. The van den Bergh test and the prothrombin time were unchanged. A cephalin-flocculation test on the blood was +++ in twenty-four and forty-eight hours. The urine gave a ++ test for albumin and a +++ test for bile. The white-cell count was 12,700.

One month after admission the pulse ranged between 90 and 70, and the temperature between 98 and 100°F. The blood protein was 7.5 gm.

per 100 cc., the albumin being 2.8 gm. and the globulin 4.7 gm., making an albumin-globulin ratio of 0.6. The blood bilirubin, according to the van den Bergh test, was slightly lower. The patient was transfused. A second paracentesis during the fifth hospital week gave 5000 cc. of similar fluid. The liver was then palpable 7 cm. below the costal border at the midclavicular line. Temperature and respirations were normal, and the pulse ranged between 60 and 100. She was discharged to a nursing home.

Final admission (nine days later). Following discharge the patient did fairly well until four days prior to re-admission, when she developed chilly sensations, irritating cough productive of small quantities of greenish sputum and a temperature of 102°F. The following day, during a bout of coughing, she suddenly felt weak, dizzy and slightly nauseated. There was some desire to move the bowels. Two days prior to re-admission she vomited black, foul-tasting "blood" on two occasions; no bright blood was seen. The day before entry she had frequent, loose, tan stools.

Physical examination was essentially the same as before. There was no peripheral or sacral edema.

The blood pressure was 130 systolic, 55 diastolic. The temperature was 100°F., the pulse 20, and the respirations 30.

The red-cell count was 2,700,000, with a hemoglobin of 7 gm. The stools gave a +++ guaiac test.

During the next two days, she had several "currant jelly" stools. She became disoriented and delirious, and died on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. WYMAN RICHARDSON: The moral of the case perhaps is, If you let demon rum get after you too much, be sure to eat enough. The interpretation of drinking "rather heavily" differs with each patient but when associated with the remark that she "stopped eating," it probably means a good deal more drinking, rather than less.

To go back to the history a moment, the question is, Did the illness begin with the febrile episode twenty-eight months before admission? It is stated that the abdomen was enlarged. If this means enlargement due to ascites, this suggests that her illness began before the febrile illness; if it was just fat, maybe not. I suspect, however, that her illness began before the febrile episode. I shall disregard the three tumors.

The patient then entered this hospital with evidence of something wrong in the liver. Physical examination revealed a big liver, which, by some observers, was thought to be nodular. It is difficult

cult to be sure about a nodular liver. Certainly one cannot feel a hobnail on a liver, but sometimes when there is tumor or the hepar-lobatum type of syphilis of the liver one can feel what might be called nodules or an irregular liver. It is significant that the spleen was palpable. Whether it is important that the knee jerks were absent, I am not certain.

The laboratory data are consistent with hepatic failure. As we have seen several times, the total protein was elevated, but the elevation was due to increase in globulin, often with a decrease in albumin. Just why it changed so quickly between the second and third determinations, I do not know.

The blood picture, so far as we are given it, is not suggestive of the ordinary type of pyogenic infection. We are told that the stools were brown; in other words, she was putting out some bile. The anemia appears to have been of the macrocytic type, since, according to the hematocrit of 40, the volume of the cells must have measured over 100 cubic microns. I should like to point out that each time the patient had a febrile episode, she seemed to get worse, until the final admission when she had sudden weakness, dizziness and nausea, obviously associated with hemorrhage. The bleeding in this case appears to have been massive and rather more than one would expect simply from the lack of prothrombin. In other words it suggests that there were varicose veins and that she ruptured such a vessel.

So we have a patient with hepatic failure, a big liver and a history of alcoholism. The diagnosis that I think most nearly fits the situation is a toxic cirrhosis and hepatitis, probably alcoholic. There is abundant experimental evidence in animals that substances that are toxic for the liver can be controlled to a considerable extent by dietary measures or the use of substances derived from food. It is also suggested that the people who get into liver trouble from drinking are deficient in their diets in some respect.

There are other conditions that have to be seriously considered. First, I shall mention the question of tumor. The bugbear of hepatoma always comes in, and usually one is wrong, because it is a relatively rare tumor. The cases of hepatoma that I have seen or discussed here have had a more clear-cut story of an antecedent portal type of cirrhosis of rather long standing. Furthermore, the presence of an enlarged spleen may be taken as evidence against other types of neoplasm, although one cannot be sure of that. There is nothing to suggest tumor except the original observation that there were three tumors. Just how they were discovered, whether by x-ray or physical examination, is not clear. In general the story

to me is perfectly easily explained on the basis of hepatic failure. The increase in the amount of failure associated with the febrile episodes is probably that commonly seen with ordinary respiratory or other epidemic infection. I am going to rule out tumor.

Another consideration that we always have to think of is syphilis. We regularly get caught on syphilis of the liver, in some cases by laying too much stress on a negative Hinton test that was not done in dilutions and in others by not paying enough attention to a positive Hinton test. This patient had a negative test. The absence of knee jerks does not necessarily mean that she had syphilis. I cannot be sure that she did not have syphilis of the liver, but I do not see anything in favor of it.

Finally, can this be subacute yellow atrophy in which regeneration had been going on for a long time? In such cases the liver may be enlarged, but I doubt that it would be as big as this one was.

To summarize, I should call this a toxic hepatitis and cirrhosis of the liver—probably alcoholic. I think the patient had varices, and probably died of hemorrhage from varices, although there can be a considerable amount of hemorrhage without one's being able to discover the source. I might add one thing. It is not too uncommon to find a peptic ulcer in association with cirrhosis of the liver. Possibly I ought to throw that in so as not to get caught, but I shall say that the hemorrhage was from varices, even though they were not demonstrated by x-ray study. So much for the liver.

The patient had a chill, fever and greenish sputum, and she may have had some pulmonary infection terminally.

DR. BENJAMIN CASTLEMAN: There was an x-ray film of the esophagus.

DR. MILFORD SCHULZ: I cannot be sure that there are any esophageal varices in this film.

DR. WILLIAM BREED: Is there no way, except by guessing, to determine the presence or absence of hepatoma on superimposed cirrhosis?

DR. SCHULZ: Sometimes a hepatoma projects through the diaphragm, forming a bulge in the upper part.

DR. CASTLEMAN: Is it not true that these patients have fever and signs of malignant disease?

DR. RICHARDSON: Not necessarily, but I think one might get a hint in the blood picture if there were widespread bone-marrow involvement.

DR. ROBERT KINNEY: Is it not worth while to examine the ascitic fluid for tumor cells?

DR. CASTLEMAN: Unless there is widespread seeding, which is extremely unusual in hepatoma, it is difficult to find tumor cells in the ascitic fluid.

DR. JACOB LERNAN: We thought that the diagnosis was alcoholic cirrhosis and that she had, in

addition, a superimposed toxic hepatitis. We also believed that hepatoma was not likely because of the relatively short duration and the rapid onset of jaundice.

CLINICAL DIAGNOSES

Alcoholic cirrhosis of liver.
Toxic hepatitis.
Bleeding from esophageal varices.

DR. RICHARDSON'S DIAGNOSES

Toxic hepatitis.
Cirrhosis of liver, probably alcoholic.
Hemorrhage from varices.
Pulmonary infection (terminal)?

ANATOMICAL DIAGNOSES

Cirrhosis of liver, alcoholic type.
Acute hepatitis, severe.
Gastrointestinal hemorrhage from gastric varix.
Jaundice.
Ascites.
Splenomegaly.
Bronchopneumonia.
Leiomyoma of uterus.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy this patient had a large liver, which weighed 2500 gm. It was hard and green. Ordinarily, a hard, green liver immediately makes one think of biliary obstructive cirrhosis. Examination of the biliary tract, however, showed that it was perfectly normal; there was no obstruction. The granularity of the liver

was that ordinarily seen in alcoholic cirrhosis. The nodules were uniformly minute, in contrast to the toxic or healed acute-yellow-atrophy type of cirrhosis, in which the nodules vary in size. The liver of alcoholic cirrhosis is usually yellowish brown, not green; however, microscopic sections showed why it was green—a marked acute hepatitis was superimposed on the alcoholic cirrhosis. The liver cells were granular and necrotic, and in many places had disappeared. The spleen was also enlarged, weighing 420 gm. The uterus contained a huge fibroid; hence, the patient did have three tumors—an enlarged liver, an enlarged spleen and an enlarged fibroid uterus.

The cause of exitus was hemorrhage into the gastrointestinal tract, but not from esophageal varices. The submucosal esophageal veins were not prominent. However, in the stomach, 4 cm. proximal to the pylorus, we found a small papilla 4 mm. long and 2 mm. in diameter, which on microscopic examination proved to be a thrombosed varix. This had ruptured and was the source of the gastrointestinal hemorrhage, rather than rupture of a vessel at the base of a peptic ulcer. Close by was a small erosion without the fibrinoid change characteristic of peptic ulceration. There were two small varices beneath this erosion, and I believe that pressure of the larger varix, plus perhaps the impaired vascularity due to the two smaller varices, accounted for the erosion. There was no gastritis such as one might expect to go along with peptic ulceration.

The patient also had terminal bronchopneumonia.

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BLOOD PLASMA

WITH the accelerating tempo of the war, the need for blood plasma is constantly increasing. In fact, the demands on the various blood-donor centers of the American Red Cross have become so great that some difficulty in obtaining the required number of donors is being experienced. Just why this is so is difficult to understand, since the total amount of plasma for which any one center is responsible can be obtained from a relatively small percentage of the surrounding population, and certainly the slight sacrifice of time and minor discomfort to the donor are greatly outweighed by the saving of the lives of literally

thousands of soldiers and sailors on extended battlefronts.

It has been said that the medical profession has failed to support the program wholeheartedly, and this statement is based chiefly on the fact that many members of a prospective donor group often refuse to give blood, with the excuse that their physicians have advised them against it. Although it is true that a few ultraconservative physicians question the advisability of repeated bleedings on the ground that no one knows the eventual effect, it is difficult to understand how the removal of moderate amounts of blood at adequately spaced intervals in a healthy and active person can do the slightest harm. The healthy professional donor who has given blood for a hundred or more transfusions is no rarity. Furthermore, in those with moderate or severe hypertension or with an excessive amount of blood, as in erythremia, blood-letting at regular periods is an accepted therapeutic procedure. In other words, there seems to be little sound evidence for believing that many of these excuses are founded on fact, but rather are "white lies" prompted by fear and conceived at the moment as the "easiest way out."

In any event, it behooves physicians to support this worthy program to the utmost. Properly couched statements concerning the value and need of plasma, the care taken at the donor centers to weed out persons who should not give blood and the relative safety and minimal annoyance of the blood-taking procedure will do much to reassure those who are hesitant to do their bit toward the saving of a life.

ROCKY MOUNTAIN SPOTTED FEVER

AN article published elsewhere in this issue of the *Journal* calls attention to the need for Massachusetts physicians to appreciate that Rocky Mountain spotted fever is endemic in the Cape Cod region. Although no cases have been reported since the summer of 1939, this is no guarantee that the infective agent has been eliminated. In fact, in areas in the West, where the disease is

relatively prevalent, cases in any one endemic area may not be reported for several years, only to recur subsequently.

It is pointed out that although the infective agent may have been introduced within the past decade by a dog carrying infected ticks or by tick-infested rabbits imported from regions where the disease is endemic, it seems more likely that a small number of local dog ticks—the insect vector of the disease to human beings—have harbored the virus for many years. However, the incidence of infection among ticks must be exceedingly low to account for the rarity of the disease.

The paucity of cases certainly does not warrant the widespread use of the specific rickettsial vaccine, but all physicians should bear in mind that any patient with an unexplained maculopapular rash and fever who has visited Cape Cod is likely to be suffering from Rocky Mountain spotted fever. This is particularly true in the case of children who are more likely than adults to have been bitten by ticks. The diagnosis can be established early in the disease by recovering the infective agent from the patient's blood, but the procedure is time consuming. After the first week of the disease, several reliable serologic diagnostic methods—agglutination tests with strains of *Proteus* (Weil-Felix reaction) or with rickettsial agents or complement-fixation tests—are available, and the latter have been shown to remain positive for several years after an attack of the disease. With these laboratory aids, together with quite characteristic clinical symptoms, diagnosis should not be difficult.

MEDICAL EPONYM

FELTY'S SYNDROME

Augustus Roi Felty (b. 1895), when a junior member of the staff of the Johns Hopkins Hospital, was the author of a paper "Chronic Arthritis in the Adult Associated with Splenomegaly and Leucopenia" in the *Bulletin of the Johns Hopkins Hospital* (35: 16-20, 1924):

The syndrome occurred in individuals of middle age (45-65), the average being 50 years. All the patients gave a history of marked loss of weight since the on-

set of symptoms. . . . The arthritic process is distinctly chronic. . . . The objective findings both by physical examination and roentgenographic study are neither widespread nor indicative of a very damaging or destructive process. . . .

In every case the spleen was palpably enlarged . . . firm but not tender. . . . In every instance there was noted a yellowish-brown pigmentation of the skin. . . .

In all cases save one there was a slight secondary anemia. . . . Most striking was the leucopenia, which was a distinctive feature in every case. The leucocyte counts varied from 1000 to 4200. . . .

The etiology is entirely obscure, though the various findings seem best accounted for as manifestations of a single disease process:

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

O'BRIEN—JOHN F. O'BRIEN, M.D., of Fall River, died June 11. He was in his fifty-eighth year.

Dr. O'Brien received his degree from McGill University Faculty of Medicine, Montreal, Quebec, Canada, in 1910. He was a member of the Massachusetts Medical Society and the American Medical Association.

SENECAL—RAYMOND E. SENECA, M.D., of New Bedford, died August 24. He was in his fifty-second year.

Born in St. Cesaire, Canada, Dr. Senecal received his degree from Boston University School of Medicine in 1917. He was on the staffs of St. Luke's Hospital and Union Hospital, New Bedford, and Acushnet Hospital and St. Anne's Hospital, Fall River. Last month he was appointed a member of the Public Health Council by Governor Saltonstall. Dr. Senecal was president of the New Bedford Medical Society at the time of his death. He was a member of the Massachusetts Medical Society, the American Medical Association, the Franco-American Civic League and the Franco-American Historical Society.

His widow, a son and two daughters survive.

STICKNEY—ROBERT C. STICKNEY, M.D., of Beverly, died September 7. He was in his forty-ninth year.

Dr. Stickney graduated from Dartmouth College and received his degree from Columbia University College of Physicians and Surgeons, New York, in 1919. He specialized in pediatrics and was a member of the staff of the Beverly Hospital and the North Shore Babies Hospital in Salem. Dr. Stickney had been chairman of the Beverly Board of Health for many years. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son and a daughter survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

THE EMERGENCY PROGRAM FOR THE CARE OF WIVES AND INFANTS OF MEN IN THE ARMED FORCES

The Children's Bureau has approved the Massachusetts plan for the emergency care of the wives

and infants of men in certain groups in the armed forces. The funds for the program are provided by the federal government and administered by the Massachusetts Department of Public Health through the Division of Child Hygiene. Payment is made for complete maternity service including prenatal care, delivery in a hospital, postnatal care and pediatric care of the infant until its first birthday. In each case the physician and the hospital agree to accept no additional fees from any other source for the patient during the period when care is authorized for payment by the Massachusetts Department of Public Health.

ELIGIBILITY

The wives of men in Grades 4, 5, 6 and 7 of the Army, Navy, Marine Corps and Coast Guard are eligible under this plan. Also included in the group are the wives of Army and Navy aviation cadets. Wives of men who are in Grades 1, 2 and 3 may receive care only if they sign a certificate of need.

APPLICATIONS

Applications for maternal or infant care must be made by the service man's wife and her physician on a special form provided by the Department of Public Health. This application should be sent immediately to Dr. Florence L. McKay, director, Division of Child Hygiene, 73 Tremont Street, Boston. Application forms are available through the Division of Child Hygiene, state district health officers, local boards of health, prenatal clinics, chapters of the American Red Cross, Army cantonments, Navy stations, visiting nurse associations, bureaus of the Travelers Aid Society and similar social service organizations.

TYPES OF CARE PROVIDED

Maternal care. The Massachusetts plan provides payment for hospital delivery only. The attending physician may be paid for one of the following:

Prenatal, delivery and post partum service (the latter includes examination of mother and infant at six weeks). Prenatal visits should include pelvic measurements and, routinely, weight, blood pressure, urinalysis and hemoglobin determinations.

Delivery and post partum service only.

Prenatal service only.

The physician who gives maternal care sends a report of service rendered on a special form to the Division of Child Hygiene with his bill for services. Payment will be made only on receipt of the bill and the report. If there is a question concerning the care given, the Technical Committee on Obstetrics will act on the case. A minimum of ten days and a maximum of fourteen are allowed in the hospital for ordinary cases. If more time is needed, special authorization must

be asked by the physician. Prenatal clinics are to be used for prenatal care where available. If the clinic regularly makes a charge to the patient, the fee may be paid through these funds.

Infant care. Payment for infant care will be made only during the infant's first year of life. Pediatric care consists of two types:

Health supervision, which is limited to one visit per month for supervision or immunization or both.
Care of the sick infant.

The sick infant may be cared for in the home or in the hospital for a period limited to three weeks. Special authorization must be requested if the period is extended beyond this point.

Where local well child conferences, with at least monthly service, are available, health supervision may be given in the conference and the conference will be paid if it regularly charges a fee.

The physician giving pediatric care sends a report of services rendered in the case on a special form to the Division of Child Hygiene, with his bill for services. Payment will be made only on receipt of the bill and the report.

Nursing care. Only bedside care by nurses licensed or eligible for license in Massachusetts may be furnished under this plan. Prenatal supervisory visits are not included for payment.

The state district health officer receives a copy of each authorization from the Division of Child Hygiene. In this way the public health nursing supervisor for the district is able to provide adequate prenatal supervisory visits, as well as bedside nursing care for the mother or infant.

Hospital care. Hospital care furnished to mothers or infants is at ward rates only. The hospital must agree to accept no other payment for hospital care from any other source during the period when care is authorized by the Massachusetts Department of Public Health.

Fees for delivery rooms, anesthesia, blood transfusions, unusually expensive drugs, ambulances and so forth are extra items and payment will be made at rates usually charged to ward patients.

PAYMENTS AUTHORIZED UNDER THIS PLAN

The attending physician may be paid according to the fee schedule that is appended. Payment for service under this plan is not retroactive. The fees allowed cover only the period after the wife signs the application blank. In emergencies, the application must be sent so as to reach the Division of Child Hygiene within twenty-four hours after the beginning of the emergency. In such cases, authorization for payment may be issued if the request is in accordance with the approved regulations.

The cost of care by the intern and resident staff of a hospital is included in the ward cost, and these

physicians will not be paid for medical service rendered to ward patients. Payment may not be made to an attending physician for service customarily provided to ward patients without reimbursement.

According to the regulations of the Children's Bureau, a fee for any one operation may not exceed the total cost of care; for example, the fee for an obstetric operation cannot be more than \$50. The attending physician cannot be paid for an operation; he must call a consultant, who will either operate or designate a specialist to do the operation. A description of the consultant service under this plan will be published at a later date, with a list of the obstetric and pediatric consultants.

STANDARDS OF MEDICAL CARE

The standards of both maternal and infant care are supervised by technical committees. The standards published in the pamphlet *Prenatal Care*, published by the Children's Bureau must be followed for prenatal care.

The physician who is to be paid for maternal or infant care must be a graduate of a Grade A medical school. Graduates of other medical schools who have had training or experience in obstetrics or pediatrics that is approved by the technical committees may be paid.

TECHNICAL COMMITTEES

The technical committees are appointed by the Commissioner of Public Health. Each committee comprises six physicians who are diplomates in their special fields.

The personnel of the Technical Committee on Obstetrics is as follows:

Dr. R. L. DeNormandie, Boston
Dr. R. J. Williams, Lynn
Dr. Raymond Titus, Boston
Dr. Louis Phaneuf, Boston
Dr. Judson Smith, Boston
Dr. Thomas Almy, Fall River

The personnel for the Technical Committee on Pediatrics is as follows:

Dr. W. R. Sisson, Boston
Dr. Stewart Clifford, Boston
Dr. Robert Moulton, Salem
Dr. Arthur Kimberly, Worcester
Dr. R. M. Smith, Boston
Dr. James Baty, Brookline

* * *

FEE SCHEDULE*

MEDICAL FEES

Maternity Care:

Complete maternity care (at least five prenatal visits, delivery and post-partum care)..... \$50.00

*The bill for service and the report of each case are to be submitted on the letterhead of the physician, hospital or nursing organization to the Division of Child Hygiene, Massachusetts Department of Public Health, 73 Tremont Street, Boston, immediately after service is given.

Delivery and post-partum care only.....	35.00
Prenatal care only (in physician's office).....	15.00
Consultation service:	
Office visit	5.00
Hospital visit when consultant is on staff.....	5.00
Home visit or visit to any other hospital.....	10.00
Travel — allowance for 25 miles or more at 4½¢ per mile	
Telephone — allowance for long-distance telephone calls	

Operations:

Obstetric or nonobstetric operations (maximum)..... 50.00

Other fees to be set by the Technical Committee on Obstetrics as need arises.

The attending physician cannot be paid for any operation. If obstetric operation is indicated, he should call on a consultant for this service. If non-obstetric surgery or other special treatment is needed, the specialist may be chosen by the consultant who is called on the case.

Infant Care (during first year of life only):

Well infant (medical supervision):

Office of private physician for complete examination at initial visit or immunization, or both, per visit..... 2.00

At well-child conference, per visit..... 50

Will be paid only to conferences regularly charging a fee; bills should be sent when the amount reaches \$5.00.

Sick infant (diagnosis and medical care):

Initial authorization for care of the sick infant can be given for a period not to exceed three weeks. A request must be made for extension of service.

First visit:

At home (maximum)..... 3.00

In office or hospital..... 2.00

Additional visits:

At home

In office or hospital..... 2.00

Maximum payment for first week of illness..... 15.00

Maximum payment for second and third weeks, per week

Maximum payment beyond third week (after special authorization is given), per week..... 6.00

Consultation service:

Office visit

Hospital visit when consultant is on staff..... 5.00

Home visit or visit to any other hospital..... 10.00

Travel — allowance for 25 miles or more at 4½¢ per mile

Telephone — allowance for long-distance telephone calls

Operations (maximum)

Other fees to be set by the Technical Committee on Pediatrics as need arises.

The attending physician cannot be paid for any operation. If operation is indicated, he should call upon a consultant. When the services of a specialist are required, the consultant will designate the specialist.

HOSPITAL FEES

In accepting the case, the hospital agrees to make no charge to patient and to receive payment from the Massachusetts Department of Public Health at the following per-diem ward rates:

Metropolitan Boston..... \$4.00

Outside Metropolitan Boston..... 3.50

Delivery room, anesthesia and unusually expensive drugs may be paid for at minimum ward rates.

The cost of blood for transfusions may be paid for at the customary rate of the hospital for ward patients.

Cost of ambulance service may be paid for at the rate of \$3 for three miles and 50 cents per mile thereafter.

Maternity cases — minimum stay of ten days, maximum of fourteen days. Extension may be had when necessary with special authorization.

Sick infant — maximum allowance of three weeks on initial authorization. Extension may be had when necessary with special authorization.

Where the prenatal clinic regularly charges a fee, \$1.50 per visit will be allowed for prenatal care.

In an emergency, when the patient must enter a hospital without authorization, application for payment for services must be made to the Division of Child Hygiene, Massachusetts Department of Public Health, within twenty-four hours.

NURSING FEES

Post partum visits per visit	\$1 25
Home delivery (maximum)	10 00
Home visit for sick infant	1 25

CANCER SYMPOSIUM

In connection with the wartime conference of the American Public Health Association, to be held at the Hotel Pennsylvania in New York City, a one day cancer symposium will be held on October 11. The participants comprise the heads of the cancer programs in thirteen states and representatives of the American Society for the Control of Cancer and the National Cancer Institute, as well as several outstanding surgeons and educators. The morning session will be devoted to a discussion of the epidemiology of cancer. At a luncheon session (\$2.25), to be held at the Hotel McAlpin, administration will be discussed. Service to cancer patients will be the subject for the afternoon session, and education in cancer, that of the evening session.

A general invitation to attend the symposium is extended to all Massachusetts physicians. Those who are interested are requested to notify the Massachusetts Department of Public Health, Room 546, State House, Boston.

MISCELLANY

COLLEGE CAMPUSES IN FIGHT AGAINST TUBERCULOSIS

Out of 860 colleges and universities that received the annual survey questionnaire of the Tuberculosis Committee of the American Student Health Association, 488 replied and 311 reported tuberculosis case finding programs in operation. In view of the heavy losses in student health personnel and other serious disturbances experienced by many schools because of the war, this report represents encouraging progress in tuberculosis control among institutions of higher education. It is significant that colleges with a definite control program discovered new cases of pulmonary tuberculosis almost eighteen times as frequently as did those colleges with no program. The following paragraphs are abstracted from a recent article (Lees, H. D. Tuberculosis among college students. *Journal-Lancet* 63:98-101, 1943) covering this subject.

The twelfth annual report of the Tuberculosis Committee of the American Student Health Association gives striking proof of the value of a tuberculosis control program as a regular part of student health service. In the 311 progressive colleges and universities (total student enrollment, 558,075) reporting such programs, 744 new cases of tuberculosis were discovered, a rate of 1335 new cases per 100,000 students. At 177 colleges (total student enrollment, 146,000) which provided no such programs, 11 new cases came to light, a rate of 75 per 100,000 students. Twenty-two food handlers were found to have pulmonary tuberculosis, and among faculty and other

administrative officers, 40 new cases were discovered, thus bringing the total of new cases found in colleges during the school year 1941-1942 to 817.

Few diseases impose such costly and far reaching penalties for public or personal failure to provide early diagnosis as does tuberculosis, yet the majority of institutions of higher education in this country still fail to employ modern tuberculosis case finding methods, which are simple and not expensive. The years of disability and suffering and the financial costs involved will reach staggering proportions, and there will be numerous deaths when ever we neglect early diagnosis of tuberculosis.

It is estimated that the complete cost of finding an undiscovered case of tuberculosis among college students on now unprotected campuses might run as high as \$166. This may seem expensive to some, who do not take into

TABLE 1 Testing Techniques in 254 Colleges Reporting Tuberculin Testing Programs (1941-1942)

DATA	NO. OF COLLEGS
Testing method	
Mantoux intradermal test	187
Vollmer patch test	24
Pirquet test	4
Combined Mantoux and patch test	3
Unspecified	11
Testing material	
Purified protein derivative	93
Old tuberculin	89
Combination of the two	1
Testing dosage	
Two dose technique	63
Single large dose	35
Single intermediate dose	37
Single small dose	37
Combination of doses	2
Testing routine	
New students and all negative reactors annually	63
New students only (no retesting)	44
New students and all seniors	29
Test of tonsils (available to all annually)	47
Other testing routines	46

account the social and economic values involved in the early diagnosis of the disease. Failure to provide modern case finding programs, however, will invariably prove far more costly to unfortunate individuals, families and communities, and can never redound to the credit of a negligent institution.

The tuberculin test provides the most sensitive and reliable index of the prevalence of tuberculous infection. In the young adult group, for the country as a whole, 21.8 per cent of students react to tuberculin, the East Coast and West Coast sections having a higher infection rate than other sections of the country.

Many of the older, largely exploded, ideas relating to tuberculosis seem still to be firmly lodged in the minds of many people. The belief is all too prevalent that early tuberculosis gives rise to early symptoms. Certain institutions report various procedures for the follow up of 'suspects'—'Weighing at frequent intervals and frequent temperature readings' are among the commoner of these. The suspects are usually those students who are markedly underweight. The committee therefore feels justified in emphasizing again the fact that the tuberculin test and the chest x-ray provide the only adequate means for the early detection of presymptomatic tuberculosis in the vast majority of cases.

Although it is not possible to speak in exact terms

of the incidence of tuberculosis as applying to the country's student population, reports available to the committee seem to indicate a decline of approximately 30 per cent in its prevalence among college students during the past six years. This may be on the conservative side, for during this period reports from many of the larger institutions conducting excellent case-finding programs indicate an extension of these procedures to include a higher percentage of their students. It is evident that more students are being examined each year and that the technics employed have improved and become more effective.

That there are various technics used in tuberculin testing is shown in Table 1. The Mantoux intradermal method continues to lead all others, while P.P.D. and O.T. are fairly even choices in testing materials. A com-

TABLE 2. X-Ray Procedures Reported by Various Institutions (1941-1942).

DATA	No OF COLLEGS
Colleges reporting tuberculin-testing program (254).	
Positive reactors x rayed once	74
Positive reactors x rayed annually	66
X ray optional (acceptance general)	60
X-ray optional (acceptance not satisfactory)	10
Other x ray routines	19
Fluoroscope used routinely to supplement x-ray	38
Fluoroscope used exclusively (chest x-ray when indicated)	12
Colleges reporting no tuberculin-testing program (57)	
Chest x-ray for all new students	22
Chest x ray for all students annually	9
Other routine x-ray programs	26

paratively large number of colleges use the two-dose technic.

Sixty-six colleges report the ideal annual x-ray of positive reactors. The various x-ray procedures reported are indicated in Table 2.

During the school year 1942-1943 the committee enlisted the co-operation of a group of eastern colleges in a study of entering students approximating 10,000 in number. Information concerning each student includes age, home address, name and location of secondary school attended and whether a private, public or parochial school; tuberculin test technic and results; and x-ray findings. It is hoped that this survey may continue without interruption for a period of ten years or longer, thus providing data indicating differences in the prevalence of tuberculous infection among students from various states and various home communities, accurate yearly comparisons, as well as supplying an index of any changes in the prevalence of tuberculous infection among students in any area.—Reprinted from *Tuberculosis Abstracts* (September, 1943).

CORRESPONDENCE

ESSENTIAL PHYSICIANS

To the Editor: Many doctors regarded as essential—though not of necessity permanently essential—to the needs of Massachusetts have recently received letters asking them to apply for commissions and to have physical examinations. The letters which they have received emphasized that no essential man will receive a commission until he has been declared available by the Procurement and Assignment Service, and the latter has been ordered by the

War Manpower Commission to declare no essential man available until a satisfactory replacement for him is found

It is clear that as the war lasts, medical officers are likely to be invalidated out from the Army and Navy, and will filter back into civilian practice. It is anticipated that many such physicians, as they return, will be able to resume the positions that they held previously in the various communities, and that as they return they may be able to take the place of men now called essential, who will thus become available for military service.

It should be re-emphasized that essential men who now apply for commissions will not receive them until they have been declared available to do so by the Procurement and Assignment Service, and that Procurement and Assignment has been directed by the War Manpower Commission to declare no such men available until, in fact, satisfactory replacement for them can be found.

REGINALD FITZ, M.D., Chairman
Massachusetts State Committee
Procurement and Assignment Service

319 Longwood Avenue
Boston 15

BOOK REVIEW

Psychoanalytical Method and the Doctrine of Freud. By Roland Dalbiez. With an introduction by E. B. Strauss, M.D. (Oxford), F.R.C.P. Translated from the French by T. F. Lindsay. 8°, cloth, Vol. 1, 415 pp. and Vol. 2, 331 pp. London: Longmans, Green and Company, 1941 \$9.00.

These two volumes, one of which is entitled "Exposition," and the other, "Discussion," are far too technical for an extended notice in this journal. Both the original French edition and the English translation have already been critically reviewed in psychiatric and psychoanalytic journals.

The general introduction by Dr. E. B. Strauss emphasizes that Freud's claim to enduring fame in the history of thought is securely established. The purpose of the author is to point out that the writings of Freud contain two serious defects. In the first place, Freud makes no clear distinction between his method and his doctrine, and secondly, the author claims that Freud is incapable of presenting his thought in a convincing form. Because of these alleged defects an attempt is made to give an objective statement of psychoanalysis.

The first volume discusses the psychopathology of everyday life, dreams, the sexual theory, the general theory of the neuroses and psychoses, the structure of the mental apparatus and the cultural applications of psychoanalysis. In the second volume, there is discussed at length the unconscious, the theories of sex and psychic causality. In both these volumes the author states that he is neither for nor against psychoanalysis, his purpose being, on the contrary, to distill from the psychoanalysis of today the results that will remain part of the science of tomorrow. His approach can, perhaps, be best summarized in his own words: "I believe that the metaphysical system which would most logically extend the results which Freud has reached, would, on the whole, be of the Aristotelean type."

(Notices on page x)

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NUTRITIONAL REQUIREMENTS IN TIME OF WAR*

RESEIL M. WILDER, M.D.†

WASHINGTON, D. C.

WITH many foods in short supply, rationing—some prefer to call it enforced food sharing—is being undertaken. Without a rationing program the only people to get enough would be the ones who have the time to raid the stores when fresh supplies come in. Any course other than rationing would lead to queues and chaos. Failure to control the use of food supplies would make impossible the shipment of food to strengthen our allies, or even to provide what is needed by the United States armies in this country and all around the globe.

There simply is not enough to give everyone all the food he wants to buy. Yet the general food position in this country is not too bad—not now, at any rate. It may be worse before the year is out. If production goals are not attained we shall soon be scraping the bottom of many a barrel. If the machinery for distribution fails to function, we shall undoubtedly be in serious trouble. And we must brace ourselves against possible sudden and unpredictable demands for food that may arise out of opportunities for new invasions, out of unexpected needs on the part of our allies or out of the necessity of providing food to starving people in reoccupied territory, to secure their help in speeding the victory against our common enemies.

However, the food position, I repeat, is now not too bad, and with reasonable good fortune in production, reasonably good management and reasonable willingness on the part of most of us to adjust consumption habits, we the people of this country will undergo only bearable hardships, even allowing for increased military needs.

Government purchases of food to feed our military forces and to help sustain the fighting strength of our allies will amount this year to roughly 25 per cent of the total production of food in this

country. Production, however, has increased enough so that despite this requisition of many million tons of food, as much is being left for home consumption as was used in the years before the war. Some commodities, including milk and poultry, are in larger supply than they were then; others, notably butter and commercially processed fruits, are shorter in supply. The figure for red meat—strange as this may sound to the many who have almost forgotten the aroma of a well-cooked beefsteak—is almost the same as that for the period 1935–1939: 124.5 pounds per capita per annum now, 126.3 pounds then. Also, the average diet, judged in terms of the nutrients provided per capita per day, is essentially the same. Were the foods distributed with perfect equity—to each according to his needs—the calories, protein, minerals and vitamins provided would fully meet for everyone the recommendations of the Food and Nutrition Board of the Division of Biology and Agriculture, National Research Council, with something of every nutrient to spare.

Perfect equity of distribution, however, is not to be expected under any system and was not attained at any time before the war. In 1935–1936 some 35 per cent of the families whose purchases of food were studied by the Bureau of Home Economics had diets that were rated as less than fair, and were the recommended daily allowances of the National Research Council to be applied as the yardstick, this percentage would be much greater. There are at least three explanations for the defective diets in 1935–1936. First, a bad nutritional environment was in part responsible. Many foods as purchased were impoverished by methods of processing, notably products derived from bread grains and some processed fruits and vegetables. Furthermore, the consumption of sugar was excessive. In such an environment it is difficult to choose a good diet without more knowledge of nutrition than most persons have. Secondly, lack by the large majority of the population of the most elementary

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 26, 1943.

†Chief, Civilian Food Requirements Branch, War Food Administration, U. S. Department of Medicine, Mayo Clinic, Rochester, Minnesota (on leave of absence).

knowledge of how to select a good diet must have contributed to many defective diets. Lastly, the food supplies available, owing largely to the low purchasing power of a high percentage of the population, were unequally distributed.

The less expensive foods are in general more impoverished by processing than are other foods. The so-called "protective foods" like milk, meat and fresh vegetables and fruits are usually higher priced. With the better money wages earned by many persons in 1942, consumption of the more expensive protective foods was greatly increased. Yet even in that year of luxury consumption (1942), analyses of family food expenditures, based on a survey of family spending and saving in war-time as published by the Office of Price Administration, revealed that at least 20 per cent of the population were not receiving annual incomes large enough to purchase the food necessary for a good diet.

It has been stated above that the provision of nutrients per capita per day obtained from the total supplies of food available for consumption by civilians in 1943 compares favorably with that for the period 1935-1939. For a large proportion of the population the nutritional situation may actually be superior. Factors that may be expected to exert a favorable influence on the position are as follows:

First, methods have been introduced for improving the nutritive quality of several important staple commodities. Chief of these is the enrichment of flour and bread with vitamins and iron. It is estimated by the milling industry that 80 per cent of the white flour is now enriched with thiamine and niacin. An order of the Food Distribution Administration requires enrichment of all white baker's bread, and approximately 90 per cent of the margarine produced is now fortified with vitamin A. Because of the fact that the cheaper commodities contribute relatively more calories to the diets of persons in low-income groups, the restorative fortifications of flour, bread and margarine that were recommended by the Food and Nutrition Board of the National Research Council have effected a wider distribution of the vitamins and minerals involved. The curtailment of supplies of sugar to approximately 70 per cent of prewar consumption is also beneficial.

Secondly, an intensive campaign of education in nutrition has been under way since the National Nutrition Conference was held in Washington in May, 1941. This campaign, directed and coordinated by the Nutrition Division, formerly in the Office of Defense Health and Welfare Services but now a part of the Food Distribution Administration, has extended into almost every hamlet in this country. It has probably not reached down

into the lower levels of literacy. Nevertheless, its effects are making themselves apparent in many homes through the selection of better foods and diets.

Thirdly, increased employment and increased incomes for large sections of the population have resulted in consumption of more of the protective foods—milk, meat, vegetables, fruits and so forth—by many persons who previously could not afford these foods. One effect of this has been to create shortages, notably of meat and butter. This experience has demonstrated for all time that the supposed surpluses of foods in the years before the war were not surpluses at all but relative deficits that were masked by inequality of distribution.

Lastly, rationing of processed fruits and vegetables and of meats, fats and cheese should have the effect of diminishing waste of food, and thus lead in turn to more effective use of the food supplies available.

Factors the effect of which may be unfavorable for the food position, especially for that section of the population with low fixed incomes, are as follows: the relatively higher cost of many foods; the abandonment or limitation of direct distribution of food and the food-stamp plan; and difficulties attending the transition to controlled distribution procedure, together with associated "black markets" and discrimination on the part of legitimate distributors in favor of former and nearby customers. Lack of satisfactory machinery for obtaining information on consumption makes it impossible to judge the net result of these opposing factors. The importance of securing current surveys of consumption in different areas by geographic position, type of employment and income level is the subject of much discussion at the present time.

Precise evaluation of the amount of poor health attributable to bad nutrition is difficult to obtain, for reasons given in a report of a special committee of the Food and Nutrition Board.¹ What evidence existed up to 1941 pointed to less than satisfactory nutrition in a large segment of every population group that had been studied.

The average American diet has been steadily improving in many ways, although not in all respects, since the last war. This improvement is believed to be a major reason for the increased height and weight of children and soldiers. The average height of the Army inductees is reported as 1 inch greater than the average for United States soldiers in World War I. On the other hand, the proportion of men currently rejected on grounds of physical disabilities has been very large. What proportion of these rejections should be attributed to malnutrition is conjectural. In

my opinion, it is high. Besides the desired surveys on food consumption, there is need for the systematic current application of several clinical tests to groups of the population to obtain a periodic appraisal of the nutritive status of the Nation.

The staff of the Civilian Food Requirements Branch of the Food Distribution Administration is responsible for watching the food position from the standpoint of civilian needs. A representative maintains close contact with each of the several commodity branches of the Food Distribution Administration so that information concerning the supply position of every food commodity is regularly available. At quarterly intervals, or more frequently, an allocation board headed by the director of the Food Distribution Administration reviews the claims for food submitted by the Army, the Navy, the Civilian Food Requirements Branch, the Office of Lend-Lease Administration and other agencies. The decisions concerning allocations are based on the recommendations of this board. Mr. Hendrikson, director of the Food Distribution Administration, takes this position:

We want our own soldiers to have all the food they need, when they need it, and where they need it. We want to go just as far as we can in meeting the food requirements of our allies. But we also want to—and must—provide American civilians with the food required to do a good job on the home front. The principle that must guide and is guiding the division among these major claimants is this: "How will it help to win the war?" Viewed in this light, the claims of all are well supported.

The civilian requirement for each commodity depends on estimates of the physiologic needs of the population as a whole, with due regard to special needs and the requirements of industry and institutions; estimates of past consumption; and judgments concerning the physiologic effects of imposed restrictions on consumption. The estimation of physiologic needs involves continuous reviewing of the entire food position. We can, for instance, do with less red meat, than the present estimated supply of 2 pounds per capita per week if poultry, eggs, dairy products and fish are in adequate supply, but when they in turn are scarce, the requirement for meat becomes more pressing. The same applies to other groups of foods. The essential consideration, from the standpoint of needs, is not the food itself but the nutrients that the food provides—the calories, protein, minerals and vitamins. However, as shortages develop in commodities now unrationed,—and presumably they will,—the necessity for withholding enough of the more essential foods to meet civilian needs will become increasingly more pressing. Furthermore, as other shortages appear

the foods involved must be added to the list of rationed foods. To arrange for rationing with the Rationing Division of the Office of Price Administration when shortages develop is also a responsibility of the Civilian Food Requirements Branch.

No system of rationing can be adjusted to satisfy perfectly the real or imagined special needs of everyone. Such a program would break down out of sheer complexity. Differential rationing has been avoided in so far as possible in every country where rationing has been tried except in Germany and Russia. Some degree of differential rationing, however, will undoubtedly be necessary for some commodities, and notably for milk. It is everywhere agreed that the need for milk is greatest in infancy and childhood, in pregnancy and lactation and in sickness. Children, pregnant and lactating women and invalids must have priority on milk even if the rest of the people go without.

This brings me to a subject in which we as physicians are professionally concerned. That is the dietary needs of invalids and hospitals. A division of the Civilian Food Requirements Branch is exclusively concerned with the problems presented by these needs. It is headed by Dr. Fred L. Adair, past chairman of the Department of Obstetrics of the University of Chicago. It has two sections. One deals with the dietary requirements of invalids and hospitals. This section will soon have the direction of a physician with experience in hospital management, who will be aided by expert dietitians. The other section deals with the requirements of pregnancy and childhood. It has been headed for some time by Dr. Sarah Deitrick, of the Children's Bureau.

The ration orders issued up to now permit wide discretion by the local rationing boards in providing supplementary rationed foods for invalids and hospitals. The door was left wide open,—although everyone has not yet discovered it,—but the time will assuredly come when abuses will necessitate correction of this situation. When this occurs, my office and the Food Rationing Division of the Office of Price Administration will want the most authoritative advice obtainable.

For this purpose the National Research Council, at the request of the director of the Food Distribution Administration, has appointed a group of eminent physicians who between them represent in an official capacity several of the professional sections of the American Medical Association; the American Diabetic Association is also represented by one of its officers. The group is called the Subcommittee on Medical Food Requirements. It is organized as a subdivision of the Committee on Drugs and Medical Supplies of the National Research Council. It will develop a procedure for

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recovery of tubercle bacilli and the reported cases of termination in frank tuberculosis. Against this concept are the facts that tubercle bacilli usually cannot be demonstrated by culture or animal inoculation and that 60 to 80 per cent of cases fail to show positive skin reactions to tuberculin. The proponents of the theory explain this by an atypical or nonacid fast phase of the bacillus. Schaumann⁴ cultivated from the lesions a group of pleomorphic organisms that he believed to represent such a phase, and they have been observed to become acid fast on passage. Several other reports⁸⁻¹² give further support to the theory that sarcoidosis is due to an atypical tubercle bacillus and that its peculiar manifestations are due to lack of tuberculin allergy. In these cases the administration of BCG to patients with sarcoidosis failed to produce tuberculin sensitivity.

According to Filho,¹³ the entire sarcoid syndrome may be found in leprosy, including skin lesions, bone changes, lymphadenopathy and anergy to tuberculin. Longcope and Pierson¹⁴ were unsuccessful in their attempt to grow fungi from the lesions.

Williams and Nickerson¹⁵ prepared from proved skin lesions an antigen that they injected intradermally into patients suspected of having sarcoidosis. In 4 cases, an erythematous reaction appeared in twenty-four hours. Such a reaction may be nonspecific, however, and Harrell⁹ was unable to duplicate these results using an extract prepared from lymph nodes. The presence of eosinophils in the blood stream in some cases suggests an allergic state. The fact that neutropenia and leukopenia may be found in the disease suggests that a virus is the etiologic agent. Harrell thinks that these patients exhibit an exaggerated nonspecific response to small amounts of a lipid fraction of a single organism or a variety of organisms. This response is analogous to the necrosis, infiltration by polymorphonuclear neutrophils and edema of the familiar allergic reaction to proteins. At the present time, however, on the basis of existing evidence, the etiology is obscure.

PATHOLOGY

The pathologic picture is characteristic, and no matter what structures are involved, the lesions are identical. The typical lesion is about the size of a miliary tubercle and is composed of large, pale staining, polygonal epithelioid cells. Small lymphocytes may be found scattered among these cells. Between nodules there is little fibrosis, but in lesions of long duration the connective tissue may be hyalinized and the reaction to Congo red stains for amyloid on this type of tissue is occasionally positive.⁹ There is no peripheral inflammatory zone about the nodules, and caseation is absent. Although necrosis is not a frequent find-

ing, small areas are occasionally seen in the central cells. Giant cells are noted at times, but are rarely numerous. When present, they are very large, with as many as twenty pale nuclei, and contain peculiar inclusions that stain intensely with hematoxylin. Giant cells occur with special frequency in the presence of degeneration of the central cells.

The solitary tuberclelike lesions do not grow in size, but increase in number, at times so much so that they form shiny, pearly gray masses that are plainly visible to the naked eye and give the appearance of tumors in the skin or masses in the spleen, liver, heart or other organs. When the lesions regress, there is a tendency to fibrosis and hyalinization. The skin, lymph nodes, lungs, bones, liver and spleen are most commonly involved, but no organ in the body is exempt. Schaumann⁴ emphasized the frequency with which lymphoid tissue is affected.

CLINICAL DATA

Clinically, sarcoidosis is characterized by widespread involvement of one or more organs, with few constitutional manifestations. Many investigators have reported that the disease occurs most often among Negroes, Puerto Ricans and Indians, whereas according to others there is no special race incidence. The disease begins insidiously in early adult life or childhood and usually pursues an indolent course. The diversity of its clinical forms is explained by the association of lesions in multiple organs. Contrariwise, seldom are all the organs involved in the same patient. Although skin lesions are frequent, the disease may be widely disseminated in their absence. The skin lesions are of several types; painless, nonpruritic, violaceous plaques with no surrounding erythema or induration, occurring most frequently on the face, arms and legs, but at times widespread; localized nodular lesions, most commonly involving the eyelids, nares, fingers and ears, and combinations of these two. Destruction and distortion of the nares may occur. The nails may be striated and brittle, and the nail beds often show the lesions. The oral and nasal mucosa may be involved.

The commonest initial finding in sarcoidosis is enlargement of the superficial lymph nodes. The adenopathy may be limited or generalized, and varies considerably in degree. The nodes are firm, rubbery, discrete and usually painless and do not adhere to surrounding tissues. The nodes most frequently involved are the preauricular, postauricular, submaxillary, submental and epitrochlear. Lymph nodes along the course of the major lymphatic vessels in the arm may be palpable, and those of normal size or only slightly enlarged may show a typical sarcoid lesion.

Pulmonary lesions are common, and several types have been described. Marked bilateral, symmetrical enlargement of the hilar and peribronchial lymph nodes is commonly the only pulmonary manifestation. In other cases, dense radiations extend from the enlarged hilar nodes into the lung fields, most often along the medial portions of the lower lobes. A frequent type is a nodular infiltration distributed bilaterally, granular in appearance and resembling miliary tuberculosis. A soft infiltration resembling caseous pneumonic tuberculosis is found at times. Honeycombing and larger cavity formations may be present. Enlargement of the lymph nodes in the superior mediastinum, especially on the right, may accompany the pulmonary lesions. X-ray films of the chest are not a guide to the severity of the disease,¹⁶ since extensive pulmonary infiltrations may be accompanied by little evidence of a disseminated process, and may resolve completely, whereas slight pulmonary involvement may be associated with extensive lesions in other organs, resulting in serious disability. There is a tendency for the pulmonary lesions to clear completely or almost completely. In a series of cases cited by King,¹⁶ resolution occurred in 60 per cent in seven weeks to three years, with an average of twenty-two months. A return of pulmonary lesions is unusual after clearing has occurred. There is some disagreement whether fibrosis may result from the healing of lesions in the lungs.

Bone lesions occur in 10 to 20 per cent of cases, usually involving the phalanges, metacarpals and metatarsals. The tarsal and carpal bones and occasionally the long bones may, however, be affected. Circumscribed cysts without change in the density of the surrounding bone represent the usual type of involvement. In other cases the bone has a latticework or reticulated appearance, with thickened trabeculae contrasting with rarefaction in the rest of the bone. The periosteum and joints are not involved. The lesions are chronic, and may resolve or progress irregularly. They do not perforate and form fistulas, but there may be inflammation and tenderness of the overlying tissues.¹⁷ Deformities and even painless mutilation of the fingers such as occur in leprosy are seen. X-ray examination of the bones is rarely positive in the absence of some obvious deformity.

Any of the structures of the eye may be involved. Conjunctivitis, keratitis, iridocyclitis or more extensive uveitis may occur. The lesions in the cornea, iris or uveal tract may heal and leave scars and synechiae. The eye involvement is most often mistaken for syphilis or tuberculosis. In some cases the parotid gland may be affected along with the eye, giving rise to the syn-

drome formerly called uveoparotid fever. The other salivary glands, or the lachrymal and mammary glands may be the seat of sarcoidosis. Involvement of muscle, peripheral nerves and the central nervous system has been noted.

Little attention has been paid to the important effects that sarcoidosis produces on the heart. Salvesen¹⁸ first recorded a case of myocardial involvement resulting in bundle-branch block. Schumann¹⁰ observed that at times heart failure results. Longcope and Fisher¹⁰ report 5 cases of sarcoidosis that showed evidence of myocardial insufficiency during life. Heart failure, arrhythmias or significant electrocardiographic changes are reported in these patients. Invasion of the pericardium by sarcoid may also occur. Cardiac function may be secondarily affected as a result of extensive pulmonary involvement, with resultant strain on the right ventricle or even right-sided heart failure.

Localization in the liver, spleen, stomach, intestines, kidney and epididymis occurs. Rotenberg and Guggenheim²⁰ report a case of sarcoidosis in which renal insufficiency and hypertension may have been due to sarcoid invasion of the kidneys.

Cases with involvement of the pituitary gland have been reported. Diabetes insipidus was present in most of them. A case of insufficiency of the anterior lobe of the pituitary gland due to sarcoid infiltration has recently been reported.²¹

Owing to the fact that groups of organs may be involved in almost innumerable combinations, a great variety of clinical syndromes result. It is to be noted, however, that all the extracutaneous lesions are characterized by their latency and their tendency to spontaneous regression, in contrast to the much more chronic behavior of the skin lesions.

It has already been mentioned that sarcoidosis is accompanied by few constitutional symptoms. Occasionally weakness, fatigability, anorexia, weight loss or arthralgia occurs. These symptoms, however, are rarely prominent. Fever may be present, usually in association with uveoparotiditis or acute progressive phases of the disease. Longcope²² emphasizes that symptoms are caused by "mechanical interference with the function of organs rather than by any form of intoxication." The sarcoid lesions by exerting pressure on normal tissue displace or destroy it. When the lesions are in the skin or superficial lymph nodes, symptoms are lacking. The opposite is true, however, when the eye, mediastinum, heart, lungs, central nervous system or other important organs are the seat of sarcoid tumorlike masses. A puzzling feature of sarcoidosis of the lung is the paucity of symptoms and signs in the presence of extensive pulmonary involvement. However, dyspnea, cough and transient chest pain may be present. Hemoptysis occurs

but is rare.²³ Secondary infection resulting in bronchopneumonia is not uncommon. Tuberculosis often develops in cases of pulmonary sarcoidosis.

LABORATORY DATA

The laboratory findings, though not constant, may be of aid in supporting the diagnosis. Anemia is not often present. The white cell count is usually normal or below normal. Marked leukopenia suggests splenic involvement, whether or not the spleen is palpably enlarged. The only abnormality of any significance in the differential count is eosinophilia. Some cases, however, never have eosinophilia, whereas in others it is transient. Some observers consider eosinophilia an index of activity. Harrell⁹ observed that showers of large mononuclear cells were present if differential counts were often repeated. The rise occurs at the expense of the polymorphonuclear leukocytes. The sedimentation rate is usually elevated during the active stage of the disease. Since, however, hyperglobulinemia may be present, the sedimentation rate cannot be used to indicate activity, for hyperglobulinemia increases the rate.²⁴

Harrell and Fisher²⁵ have discussed the changes in blood chemistry. They found the blood calcium to be normal or above normal and the serum phosphatase usually increased in the active phase. The latter finding could not be correlated with the duration of the illness or the site or extent of the lesions. Nonprotein nitrogen and phosphorus levels are normal. The total cholesterol is low or normal. The plasma proteins show an interesting variation. The globulin fraction is commonly elevated sufficiently to raise the total plasma protein. When the total proteins are within normal limits, the globulin fraction is often larger than normal and in excess of the albumin fraction. The plasma albumin is normal or slightly decreased. The urine is usually normal, although Harrell⁹ in 2 cases found a substance resembling Bence-Jones protein in its solubility at the boiling point.

COURSE OF DISEASE

Sarcoidosis is characterized by a chronic, usually benign course and periods of remission. Complete cure may occur. The two shortest reported periods of recovery are five and twenty seven months. Recovery may be spontaneous, or simultaneous with the development of intercurrent tuberculosis. The prognosis is good, and the disease is usually not fatal except when vital organs are involved.

DIAGNOSIS

Sarcoidosis must be differentiated from Hodgkin's disease, lymphosarcoma, bronchiolitis fibrosa obliterans, erythema nodosum, leukemia, fungous

infection, tuberculosis, especially the noncaseous variety, and syphilis. The correct diagnosis is usually made by exclusion or biopsy. When enlargement of lymph nodes predominates, the disease must be differentiated from follicular lymphoma blastoma (giant lymph follicle hyperplasia).²⁶ This is a relatively benign disease of the lymphatic system characterized by lymphadenopathy (due to dimensional and numerical hyperplasia of the follicles), splenomegaly (60 per cent of cases), a normal blood picture, absence of cachexia, a long course and a prompt response of the lymph nodes and spleen to x-ray therapy in the early stages of the disease. The pathologic picture is characteristic.

TREATMENT

Various types of treatment have been advocated. Arsenicals, iodides, leprosol, tuberculin, hyperpyrexia, gold salts, roentgen rays²⁷ and radium have been used without great success. Carbon dioxide snow and x-ray therapy have, however, been of some value in the treatment of skin lesions. Longcope²² has observed a favorable effect of ultraviolet irradiation on the skin lesions and superficial lymph node enlargement. Others have noted no benefit from its use. As a matter of fact, it is difficult to evaluate any form of therapy in view of the natural tendency of the disease to undergo spontaneous remission. Until more is known of the etiology and pathogenesis of sarcoidosis, treatment must remain empirical.

CASE REPORTS

CASE 1. A 19-year-old Negroess developed a mild upper respiratory infection. For the ensuing 2 weeks, she had moderate weakness, nonproductive cough and considerable dyspnea even while at rest. X-ray examination of the chest led to a diagnosis of pulmonary tuberculosis and the patient was sent to a sanatorium. While there, she continued to be weak and dyspneic. Examination of the sputum was repeatedly negative for tubercle bacilli and fungi. Intradermal tuberculin tests with PPD (purified protein derivative), first and second strengths were negative. A splenic puncture was negative. After 1½ months, the patient was transferred to the Gallinger Municipal Hospital for further studies.

Her past history disclosed that she had been frail and short of breath for as long as she could remember. As a child, she had been unable to play with other children because of dyspnea.

At the time of admission to the hospital, the patient appeared asthenic. While she was lying flat in bed, the breathing was rapid and shallow. The temperature was 99°F, the pulse 80 and regular, and the respirations 36. A firm movable lymph node 1.5 cm in diameter was felt 7 cm above the middle third of the right clavicle. The heart was normal. Subcrepant rales were heard over the upper halves of both lungs, and there was bronchial breathing over the upper portion of the right and left lower lobes and over the right middle lobe. The

spleen was felt one fingerbreadth below the costal margin and was firm and smooth.

An x-ray film of the chest (Fig. 1) showed diffuse infiltration and mottling throughout both lungs. In the



FIGURE 1. Case 1.

Note the diffuse infiltration and mottling with small areas of cavitation in the upper lobes and prominent hilar shadows.

upper lobes there were small areas of cavitation. The hilar shadows were prominent. Films of the hands and feet were negative. The red-cell count was 5,530,000, and the white-cell count 5800, with 64 per cent neutrophils, 30 per cent lymphocytes and 6 per cent monocytes. The serum albumin was 3.39 gm., and the serum globulin 3.02 gm. per 100 cc. Urinalysis was negative. Biopsy of the cervical lymph node resulted in a diagnosis of sarcoidosis.

The patient's course was uneventful until the 17th hospital day, when she suddenly became orthopneic and cyanotic. The temperature rose to 103°F. and the pulse to 150. On the following day, the liver was tender and extended four fingerbreadths below the costal margin. The venous pressure was 220 mm. of saline solution and rose to 270 mm. on pressure in the right upper quadrant. The arm-to-tongue circulation time, measured with 10 per cent magnesium sulfate, was 31 seconds. The dyspnea and cyanosis continued and the patient died on the 18th hospital day.

Autopsy. The right ventricle of the heart was hypertrophied and dilated. The right auricle was dilated. There was no evidence of sarcoid involvement of the myocardium. The pericardium was normal. Both lungs were studded with grayish masses. On sectioning the lung, these masses were not necrotic and at the apices small cavities with smooth walls were seen. There was no evidence of caseation. The microscopic sections showed typical sarcoid lesions. Occasional giant cells were seen in these sections. The spleen weighed 550 gm. and contained numerous large gray masses 1 to 3 cm. in diameter. Microscopic examination showed evidence of sar-

coidosis. The liver weighed 1700 gm. Small gray masses about 0.5 cm. in diameter were seen on the surface and on a cut section. The lesions of sarcoidosis were seen on microscopic examination. The pancreas, adrenals and gastrointestinal and genitourinary tracts were normal.

Comment. This case represents sarcoidosis involving several organs. The clinical and pathological findings suggested chronic strain of the right ventricle due to severe pulmonary disease, and the immediate cause of death was acute failure of the right ventricle.

CASE 2. A 22-year-old Negro developed a mild, non-productive cough and dyspnea on exertion 3 weeks before admission. On the advice of his physician, an x-ray film of the chest was taken, and on the strength of this the patient was referred to the hospital with a diagnosis of far-advanced pulmonary tuberculosis. The past history was negative except for a corneal ulcer at the age of 10.

At physical examination the patient looked well developed, well nourished and healthy. The only positive

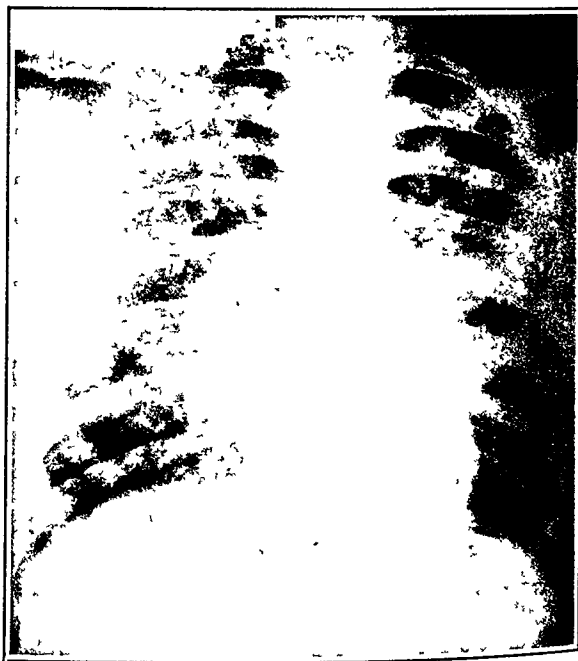


FIGURE 2. Case 2.

Note the bilateral enlargement of the hilar nodes and diffuse mottled infiltration throughout both lungs.

findings were a right corneal scar 0.3 cm. long, bilaterally palpable epitrochlear lymph nodes 1 cm. in diameter and occasional sibilant rales in the right hemithorax.

The red-cell count was 4,900,000, and the white cell count 4000, with 57 per cent neutrophils, 39 per cent lymphocytes, 3 per cent monocytes and 1 per cent eosinophils. Examinations of six sputums and one gastric washing were negative for tubercle bacilli. The intradermal tuberculin test with P.P.D., first strength, was negative, but the test was slightly positive with P.P.D., second strength. The serum calcium was 12 mg. per 100 cc., the serum albumin 5.27 gm., and the serum globulin 3.35 gm. An x-ray film of the chest (Fig 2) showed bilateral enlargement of the hilar lymph nodes and a diffuse, mottled infiltration throughout both lungs.

Biopsy of an epitrochlear lymph node revealed findings typical of sarcoidosis.

As the patient felt well, he was discharged to return each month for a check up examination.

Comment This case is quite typical of sarcoidosis with diffuse pulmonary involvement, few symptoms and no constitutional reaction. The corneal ulcer at the age of 10 may have been due to sarcoidosis.

CASE 3 A 42-year-old Negress was admitted to the hospital complaining of cough and fever. Ten days previously, she had a severe chill followed by fever. For the ensuing 10 days, she remained in bed because of weak

fingers were deformed. There was slight dullness over both upper lobes anteriorly. Over the right hemithorax and left upper lobe, sibilant and sonorous rales were heard. Bronchial breathing and subcrepitant rales were present over the right upper lobe. At both bases subcrepitant rales were heard.

The red-cell count was 3,500,000 and the white cell count 7000, with 58 per cent neutrophils, 23 per cent band forms, 12 per cent monocytes, 6 per cent lymphocytes and 1 per cent eosinophils. Urinalysis was negative. The serum albumin was 2.17 gm and the serum globulin 4.76 gm per 100 cc. Intradermal tuberculin tests with PPD, first and second strengths were negative. The sputum was negative for tubercle bacilli on six occasions. An x-ray film of the chest (Fig. 3) showed diffuse mottling and fibrosis throughout the greater portion of the right lung and the upper half of the left lung. There were many small cavities in the left upper lobe and a large fluid-containing cavity 4 cm in diameter in the right upper lobe. X-ray films of the hands and feet (Fig. 4)



FIGURE 3 Case 3

Note the diffuse infiltration and cavity formation most marked in the upper halves of both lungs

ness, dyspnea and a severe, dry cough. There were no chest pains, hemoptysis or night sweats.

The past history revealed that the patient had been short of breath for 1 year. The dyspnea had become progressively but only slightly worse until the onset of the present illness, when it became so severe that the patient could not lie flat in bed. Six years before admission a nodular rash had appeared on the cheeks and nose. A biopsy of the skin taken at the Dermatology Clinic of the Georgetown Hospital had established the diagnosis of sarcoid.

At physical examination the patient looked seriously ill. The temperature was 102.5°F, the pulse 120 and respirations 40. On both cheeks and spreading across the bridge of the nose was a dark red nodular lesion. The nares were enlarged and distorted. A similar lesion was present on the right upper eyelid, the right side of the lower jaw and the right elbow. Several submaxillary lymph nodes were enlarged, firm and freely movable. The right index finger and the left ring finger were broader than the others. The distal phalanges and nails of these

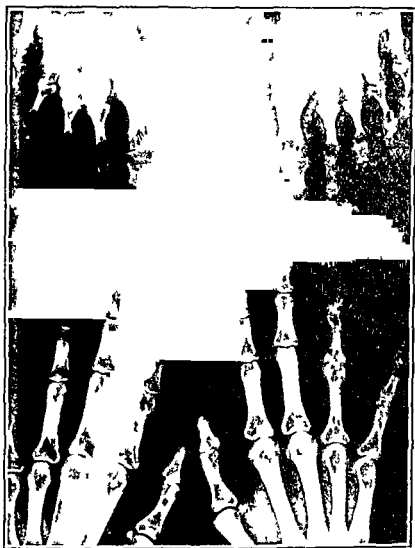


FIGURE 4 Case 3

Note the many sharply punched-out areas most marked in the phalanges of the right index and left ring fingers

showed many sharply punched-out areas indicating bone resorption in the phalanges of the right index and left ring fingers and in several of the carpal and metacarpal bones. An electrocardiogram showed low T waves in Leads 1 and 4, which were suggestive of myocardial damage.

The patient was given sulfadiazine. After 4 days the temperature, pulse and respirations were normal. The chest findings were unchanged except for the disap-

pearance of the basal rales. Re-examination of the chest by x-ray 10 days after admission showed no appreciable change except that the cavity in the right upper lobe was empty. The temperature remained normal and the patient was symptom free at discharge on the 25th hospital day.

Comment. This is a case of sarcoidosis with skin, bone and pulmonary lesions and a superimposed pneumonia that responded to chemotherapy.

CASE 4. A 46-year-old Negro had transient pain in the left side of the chest in May, 1941. The pain was dull and slightly intensified by deep breathing. A physician sent him to the District of Columbia Chest Clinic, where an x-ray film of the chest was taken. He was then sent to the Glenn Dale Sanatorium.

The past history revealed a loss of 20 pounds during the preceding 5 months. This the patient attributed to hard work as a laborer. He had been in a tuberculosis sanatorium for 5 months in 1931 because of "swollen glands" in his neck. At that time he noticed a skin lesion above the left clavicle.

He remained at the Glenn Dale Sanatorium until November, 1941, and left against advice. While there he gained 17 pounds and was symptom free. All sputum examinations were negative for tubercle bacilli. From November, 1941, until May, 1942, the patient stayed at home and continued to feel perfectly well. During this



FIGURE 5. Case 4.

Note the numerous areas of infiltration and honeycombing throughout the greater portion of the left lung and the middle third of the right.

period frequent sputum examinations were negative for tubercle bacilli. In May, 1942, he was advised to enter the Gallinger Municipal Hospital for further study.

At physical examination the patient was slightly obese and appeared to be in excellent health. There were dark-red skin lesions in patches above the left clavicle. The lesions were nonscaly, nonindurated and raised in plaques. There was slight diminution in breath sounds over the left lower lobe. The remainder of the examination was negative.

An x-ray film of the chest (Fig. 5) showed numerous areas of infiltration and honeycombing throughout the greater portion of the left lung and middle third of the right lung. At the left base there was evidence of thickened pleura. X-ray films of the hands and feet were negative. Examinations of the sputum and gastric washings were repeatedly negative for tubercle bacilli. Sputum culture for fungi was negative. An intradermal tuberculin test was positive. The sedimentation rate (Ernst-Rourke method) was 1.55 mm. per minute (normal, 0.35 mm.). The serum albumin was 2.92 gm., the serum globulin 5.16 gm., and the serum calcium 11.8 mg. per 100 cc. The red-cell count was 4,000,000, and the white-cell count 5600, with 39 per cent neutrophils, 51 per cent lymphocytes, 7 per cent monocytes, 2 per cent eosinophils and 1 per cent basophils. A biopsy of the skin lesion showed sarcoid.

Comment. This is a case of sarcoidosis with skin and pulmonary lesions. The diagnosis was suggested by the evidence of diffuse pulmonary disease resembling tuberculosis in the absence of symptoms and signs of that disease.

CASE 5. A 24-year-old Negro was admitted complaining of swollen femoral and axillary lymph nodes. Ten months previously, he noticed slight, painless swelling of the femoral lymph nodes on both sides. A short time later, he noticed similar swelling of the axillary lymph nodes. These groups of nodes gradually became larger. The bulging of the femoral nodes through his trousers caused him considerable embarrassment, and for this reason he sought admission to the hospital.

At physical examination the patient looked well developed, well nourished and healthy. The preauricular, axillary, cervical, epitrochlear, inguinal and femoral lymph nodes were enlarged. They were discrete, rubbery, movable and nontender. The axillary nodes were about 3 cm. in diameter and the femoral nodes about 6 cm. in diameter. Over both knees and the back of the neck were hard, salmon-colored plaques 0.5 to 1.0 cm. in diameter. The remainder of the examination was negative.

An x-ray film of the chest (Fig. 6) showed bilateral enlargement of the hilar lymph nodes. Films of the hands and feet were negative. The red-cell count was 5,580,000, and the white-cell count 3600, 69 per cent neutrophils, 27 per cent lymphocytes, 3 per cent eosinophils and 1 per cent basophils. Urinalysis was normal. The corrected sedimentation rate (Wintrobe method) was 38 mm. per hour. The serum albumin was 4.85 gm., and the serum globulin 3.96 gm. per 100 cc. Intradermal tuberculin tests (P.P.D., first and second strengths) were negative. A biopsy of a lymph node revealed sarcoid.

The patient was given x-ray therapy to the chest and femoral regions, with resultant slight reduction in the size of the lymph nodes. Six weeks after the completion of x-ray therapy the patient noticed some newly enlarged inguinal lymph nodes. At that time, however, the nodes were very painful and tender. They were fluctuant, inflamed and draining a sanguinopurulent fluid. The temperature was 102°F. There was no penile lesion. A Frei test was strongly positive. The drainage continued for 2 weeks, during which time the temperature fluctuated between 100 and 102°F. At the end of this period the lymph nodes were hard and fixed. Biopsy of one of the inguinal nodes resulted in a diagnosis of lymphopathia venereum.

Comment This case represents one of sarcoidosis with superimposed lymphopathia venereum. The lymph nodes in sarcoidosis do not break down and the overlying skin does not show evidence of inflammation. In lympho-

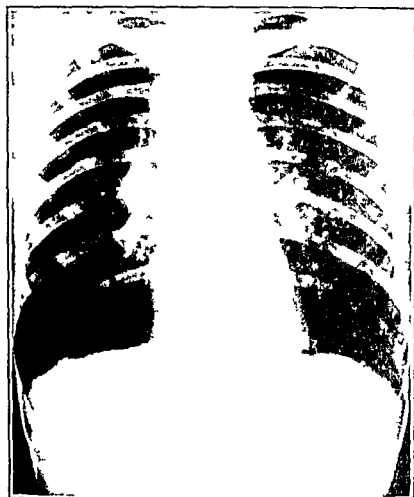


FIGURE 6 Case 5

Note the bilateral enlargement of the hilar lymph nodes and mediastinal nodes

pathia venereum, there is also an elevation of the serum globulin, which has suggested to some observers an etiologic background similar to that of sarcoidosis. In Longcope's²⁰ series of cases, however, Frei tests were done in 8 cases with a positive result in only 1.

CASE 6 An 18-year-old Negroess was admitted complaining of cough and mild chest discomfort of 24 hours duration. Her cough was productive of mucoid sputum that was occasionally blood tinged. Slight dyspnea on exertion had been present since the onset of the present illness. Her appetite had been poor for 3 months, and during this time she had lost an unspecified amount of weight.

Physical examination revealed a well developed and fairly well nourished patient who was moderately dyspneic. The temperature was 99°F, the pulse 100, and the respirations 36. The blood pressure was 110/60. The scleras were icteric. Examination of the chest was negative except for slight diminution of breath sounds over the right upper lobe. The remainder of the examination was negative.

X-ray examination of the chest showed no definite evidence of infiltration of the lungs, but there was a generalized accentuation of the bronchovascular shadows. Overlying the right upper lobe there was a hazy density that was interpreted as due to a pleural reaction. X-ray films of the hands and feet were negative. A blood Kahn reaction was ++. Sputum examinations were repeatedly negative for tubercle bacilli. Intradermal tuberculin tests

(PPD, first and second strengths) were negative. The urine showed a strong reaction for bilirubin. The red cell count was 5,300,000, and the white cell count 6850, with a normal differential count. The Van den Bergh reaction was direct, and there was 84 mg of bilirubin per 100 cc of blood. The icteric index was 60. The serum albumin was 2.53 gm, the serum globulin 2.26 gm, and the blood cholesterol 166 mg per 100 cc.

The cough and chest pain subsided after 2 days. The temperature became normal on the 3rd day. At that time the patient was entirely symptom free except for slight dyspnea. Two weeks after admission an x-ray film of the chest (Fig 7) showed diffuse irregular areas of infiltration throughout both lung fields. She felt quite well and a physical examination was negative except for slight icterus. The icteric index was 28. Subsequent x-ray examination of the chest 10 and 20 days later showed no change from the second examination.

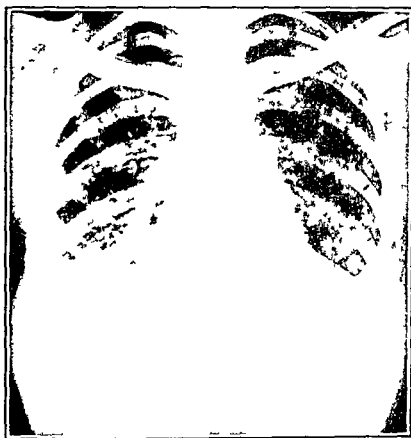


FIGURE 7 Case 6

Note the diffuse irregular areas of infiltration throughout both lungs

The patient was discharged on the 45th hospital day without any symptoms or signs, but with x-ray evidence of diffuse pulmonary infiltration. She returned at 3-week intervals for check-up examinations. After leaving the hospital she continued to feel perfectly well. X-ray examination of the chest showed no change.

Comment In this case of sarcoidosis the pulmonary lesions developed while the patient was under observation. Although no acute symptoms are attributed to pulmonary sarcoidosis, few cases have been observed during the period of development of the lesions. The symptoms in this case may have been due to sarcoidosis or may have been manifestations of a superimposed inflammatory process.

CASE 7 A 39-year-old Negro was admitted because of cough and dyspnea. Six weeks before admission, he coughed up a small amount of blood streaked sputum for the first time. Three weeks later, he developed a cough,

productive of mucoid sputum that was occasionally blood tinged. He continued to work for the next two weeks and then was forced to stop because of several episodes of chilliness, profuse perspiration and dyspnea.

The past history was entirely negative except for the loss of 15 pounds during the preceding year.

At physical examination the patient appeared well developed and well nourished but moderately dyspneic. The

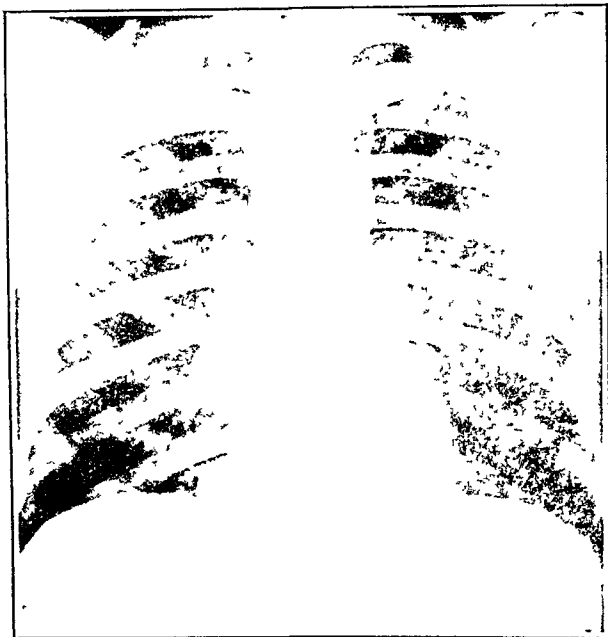


FIGURE 8. Case 7.

Note the small nodular areas of infiltration throughout both lungs.

temperature was 102°F., the pulse 100, and the respirations 36. There were numerous subcrepitant rales over the lower halves of both lungs. The remainder of the examination was negative.

An x-ray film of the chest (Fig. 8) showed discrete and coalescent small nodules symmetrically distributed throughout both lungs. X-ray films of the hands and feet were negative. Examinations of the sputum and gastric washings were negative for tubercle bacilli. A culture of the sputum was negative for fungi but showed sputum Types 10 and 18 pneumococci. Urinalysis was negative. The red-cell count was 4,000,000, and the white-cell count was 4200, with 61 per cent neutrophils, 36 per cent lymphocytes and 3 per cent monocytes. The serum albumin was 5.75 gm. and the serum globulin 4.11 gm. per 100 cc. An intradermal tuberculin test with P.P.D., first strength, was negative, but with second strength it was weakly positive.

The temperature remained elevated for the ensuing 2 weeks, ranging between 103 and 100°F. The cough and dyspnea improved. An x-ray film of the chest showed the same discrete nodules throughout both lungs. The coalescence previously described was no longer present. Examination of the chest at this time was negative.

During the next week the patient felt entirely well except for slight dyspnea on exertion. He remained under observation for the next 4 months, with no change in the chest x-ray or physical examination. During this period he was symptom free and gained 10 pounds. He was

discharged and went back to work as a garbage collector. He has since been seen at monthly intervals. When last seen 7 months after discharge he was feeling entirely well and had gained 20 pounds. X-ray examination of the chest showed slight clearing of the discrete nodular areas of infiltration.

Comment. This is a case of pulmonary sarcoidosis with a superimposed acute inflammatory process that subsided after 2 weeks.

CASE 8. A 52-year-old Negress was admitted because of dyspnea. She had been in excellent health until 1 year before admission, when she noticed dyspnea following exertion. She consulted a physician, who attributed the dyspnea to heart failure. No benefit resulted from treatment with digitalis. The dyspnea became more severe, and she was admitted for further study.

The past history was negative except for a loss of 16 pounds during the year preceding entry.

Physical examination was completely negative.

An x-ray film of the chest (Fig. 9) showed diffuse in-

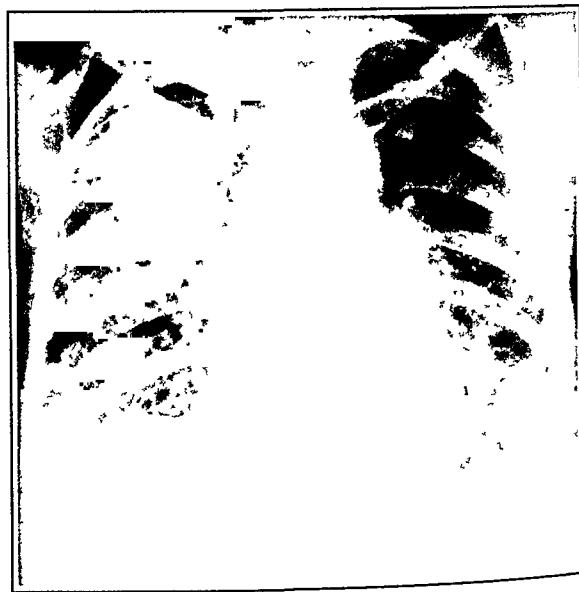


FIGURE 9. Case 8.

Note the diffuse mottled infiltration throughout both lungs.

filtration throughout all portions of both lungs. Films of the hands and feet were negative. Examinations of the sputum and gastric washings were repeatedly negative for tubercle bacilli. A culture of the sputum was negative for fungi. The red-cell count was 4,730,000, and the white cell count was 4400, with 39 per cent neutrophils, 52 per cent lymphocytes, 9 per cent monocytes, 1 per cent eosinophils and 2 per cent basophils. Urinalysis was negative. The serum albumin was 2.5 gm., the serum globulin 4.3 gm., and the serum calcium 12.5 mg. per 100 cc. An intradermal tuberculin test with P.P.D., first strength, was negative, but with second strength it was weakly positive.

The patient remained symptom free except for dyspnea on exertion. X-ray films of the chest taken 2 and 4 months after admission showed no change.

CASE 9. A 27-year-old Negro had a chest x-ray film taken as a part of a routine examination. He had no

complaints and his physical condition seemed excellent. The film (Fig. 10) showed bilateral symmetrical enlargement of the hilar lymph nodes and small discrete nodules throughout both lung fields. There were also enlarged lymph nodes in the superior mediastinum on the right

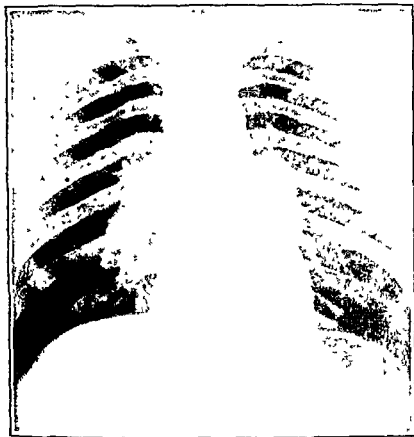


FIGURE 10. Case 9.

Note the bilateral symmetrical enlargement of the hilar lymph nodes and the small nodules throughout both lungs.

side. The x-ray examination was repeated 2 and 4 months later and showed no change, and the physical examination remained negative.

Examinations of the sputum and gastric contents were negative for tubercle bacilli. The red-cell count was 5,000,000, and the white-cell count 5200. The serum globulin was 2.5 gm., and the serum albumin 4.5 gm per 100 cc. The sedimentation rate (Ernstene-Rourke method) was 1.1 mm. per minute. Intradermal tuberculin tests (P.P.D., first and second strengths) were negative.

Comment. Although in this case and in the three preceding cases the diagnosis of sarcoidosis was not proved by biopsy, the clinical course and x-ray findings in each case favored this diagnosis.

CASE 10. A 20-year-old Negress developed a nonproductive cough and dyspnea on exertion in June, 1942. She was seen by a physician, who said that she had whooping cough and prescribed various cough medicines. The cough and dyspnea continued, but were not very disturbing. In October, 1942, the patient experienced lower abdominal pain, a vaginal discharge and fever. A diagnosis of acute salpingitis was made by a physician, and one of the sulfonamide drugs was administered. Within 5 days the manifestations of acute pelvic inflammatory disease subsided. During the ensuing 4 months the cough and dyspnea became more severe. The weight in June, 1942, was 196 pounds and in February, 1943, it was 141 pounds. Because of this weight loss, cough and dyspnea, the patient was referred by her physician to a hospital. Following x-ray examination of the chest she

was transferred to the Gallinger Municipal Hospital with a diagnosis of miliary tuberculosis.

The past history revealed "rheumatism" at the ages of 13 and 15. Since the age of 17 the patient had had episodes of polyarthritis lasting several days. An appendectomy had been performed at 13 years of age, and a tonsillectomy at 14. She had had a 6-month spontaneous abortion at the age of 16.

At physical examination the patient was well nourished and well developed and did not appear to be ill. She was slightly dyspneic and coughed every few minutes. The temperature was 98.6°F, the pulse 100, and the respirations 35. The only positive findings were occasional subcrepitant rales over the lower halves of both lungs and bilaterally palpable epitrochlear and axillary lymph nodes 1 cm. in diameter.

An x-ray film of the chest (Fig. 11) showed diffuse, discrete and coalescent miliary nodules throughout both



FIGURE 11 Case 10.

Note the miliary nodules throughout both lungs

lungs. In the right superior mediastinum there was a large lymph node and in both hilar areas the infiltration was more homogeneous. X-ray films of the hands and feet were negative. The red-cell count was 4,980,000 and the white-cell count 6100, with 51 per cent neutrophils, 31 per cent lymphocytes, 5 per cent eosinophils and 1 per cent basophils. Examinations of five sputums and one gastric washing were negative for tubercle bacilli. Culture of the sputum was negative for fungi. Intradermal tuberculin tests (P.P.D., first and second strengths) were negative. The serum calcium was 112 mg., the serum albumin 4.77 gm. and the serum globulin 3.72 gm. per 100 cc. Urinalysis was negative. The sedimentation rate (Ernstene-Rourke method) was 0.6 mm. per minute. A blood Kahn reaction was negative. A biopsy of the right epitrochlear lymph node showed the typical findings of sarcoid.

The patient remained in the hospital for 7 weeks. During that time she gained 10 pounds and felt well except for exertional dyspnea and cough. The temperature was normal throughout her stay. One week after discharge she returned to the hospital complaining of severe malaise,

fever, sore throat and headache of 24 hours' duration. On the evening before admission she had had a shaking chill.

At physical examination the patient was seen to be acutely ill. The temperature was 104°F., the pulse 160, and the respirations 70. Subcrepitant rales were heard throughout both lung fields. A culture of the sputum showed Type 7 pneumococcus, and a blood culture was negative. The remaining laboratory studies showed no significant change from the previous admission. X-ray examination of the chest showed no appreciable change from the previous examination with the exception of a slightly greater degree of coalescence of the nodules.

The patient was given sulfadiazine, and within 48 hours the temperature was normal, the pulse 100 and the respirations 34. She has remained afebrile and asymptomatic with the exception of slight cough and exertional dyspnea.

Comment. This case shows the ease with which sarcoidosis may be mistaken for miliary tuberculosis from the roentgenologic point of view. On the other hand, the absence of severe constitutional manifestations in the presence of diffuse pulmonary disease should lead one to the correct diagnosis. The superimposed bronchopneumonia is not an uncommon finding in sarcoidosis. The polyarthritis may also have been due to sarcoidosis.

SUMMARY

The concept of sarcoidosis as a generalized systemic disease is traced in the literature, and its cause and manifestations are discussed.

Arguments for and against a tuberculous origin of the disease are presented. The syndrome is also found in leprosy.

The fact that neutropenia and leukopenia may occur suggests that a virus is the etiologic agent, but the etiology remains obscure.

Clinically, sarcoidosis is characterized by widespread involvement of organs, with few constitutional manifestations. The commonest initial finding is enlargement of lymph nodes. Pulmonary and bone lesions are common. There is wide variation of syndromes.

The laboratory findings, course, diagnosis and treatment are discussed.

Ten typical cases are briefly reported.

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CLINICAL NOTES

THE USE OF DALIBOUR'S WATER IN THE TREATMENT OF SKIN DISEASES

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DALIBOUR'S water has been used by French dermatologists in the treatment of traumatic wounds and pyogenic infections of the skin for almost two hundred and fifty years. A weak solution of copper sulfate and zinc sulfate, it is an excellent astringent, bacteriostatic and deodorant. It deserves more widespread use in this country than it is receiving, both because of its obvious intrinsic worth and because in dermatological therapy it can be substituted with advantage for many of the other heavy metals—aluminum, silver and so forth—that are needed in the war effort.

The name has been spelled many different ways, including "Aullebourst," "D'alibourst" and "D'albourt." In all official papers, however, the spelling has been "Dalibour," and the latest edition of the French pharmacopoeia has reaffirmed this form.

The water or solution was first described by Jacques Dalibour in 1700.² The formula of the "eau de merveille" was kept a family secret until 1812, when its composition was revealed in the *Formulaire Magistrale*. It is as follows:

R	Copper sulfate	0.1 gm
	Zinc sulfate	0.4 gm
	Safranine	0.1 gm
	Camphor water	10 cc
	Water	q s ad 100.0 cc

Sig Dilute with three or four parts of water and apply as a wet dressing or compress

When large quantities are to be used, a ten-times concentrated solution is more convenient and economical. This should be diluted before use with twenty to forty parts of water.

The solution is clear, odorless and pink, is as astringent, and has a mild metallic taste. The pH varies from 5.3 to 6.3.

Combes³ has said

The logic of Dalibour's reasoning in compounding this solution is simple and clear. The local therapeutic value of copper sulfate and zinc sulfate was recognized by physicians many centuries before boric acid and aluminum acetate were known. Blue or Roman vitriol water in the fourteenth and fifteenth centuries was extolled as a local wet dressing in cutaneous inflammations and impetigo. The same may be said of white vitriol, which found its broadest use as a

collyrium in inflammations of the conjunctiva. Copper sulfate, in addition to possessing local stimulating and astringent properties, even in high dilutions is bacteriostatic and fungicidal.

Camphor is highly prized in the household as a local sedative. Aqua sedativa is an old item in the *National Formulary*, its antipruritic and sedative properties being dependent upon its camphor content . . .

The simultaneous application of copper and zinc sulfates and camphor by means of Dalibour water affords us an effective bacteriostatic, astringent and sedative solution for use as a wet compress.

Many modifications of the original formula are possible. The addition of 1 per cent gentian violet or 1 per cent brilliant green increases the bacteriostatic properties. Omission of the safranine permits the dispensing of a light blue solution. From 0.5 to 1.0 per cent of formalin may be included to enhance the astringent effect, or alcohol may be substituted for part of the water to further the solution's drying and astringent characteristics. Many similar alterations can be made and will readily come to mind.

When employed in the form of a wet dressing or wet compress, Dalibour's water is an effective remedy for superficial pustular infections of the skin. It is especially useful in the therapy of secondarily infected epidermophytosis, scabies or pediculosis corporis. It is equally valuable in the treatment of impetigo contagiosa, nummular eczema, superficial erosions and varicose ulcerations. Such use effects prompt control of the infectious process, thus permitting early definitive therapy for the underlying condition—scabies, epidermophytosis and so forth.

The water can be incorporated readily in such widely used preparations as lanolin, zinc oxide paste N F, and bentonite paste, or in one of the newer oxycholesterin or glyceryl monostearate creams. The following formulas are suggested:

R	Copper sulfate	0.04 gm
	Zinc sulfate	0.15 gm
	Water	3.00 cc
	Lanolin	10.00 gm
	Zinc oxide paste N F	q s ad 30.00 gm

Sig Apply to oozing parts

R	Copper sulfate	0.3 gm
	Zinc sulfate	0.9 gm
	Urea	12.0 gm
	Aerosol OT (25 per cent)	0.2 gm
	Bentonite	20.0 gm
	Water	q s ad 120.0 cc

Sig Apply to ulcers

As a deodorant it is unsurpassed for the therapy of severe odorous cancerous lesions, condyloma acuminatum or epidermophytosis. In weak dilutions, either as a compress, in a vanishing cream or applied by atomizer to the axilla before bed-

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time two or three times a week, it is effective in the relief of hyperidrosis and bromidrosis.

A mixture of copper sulfate and zinc sulfate may be prescribed in powder form for the bath. Thirty parts of copper sulfate and 90 parts of zinc sulfate are mixed and pulverized, and from a teaspoonful to a tablespoonful of the powder is dissolved in water and added to the bath. Such baths are astringent and bacteriostatic and efficiently remove odor from patients suffering with pemphigus vulgaris, ulcerating cancer or other malodorous conditions. The patient is allowed to remain in the tub from ten to thirty minutes. Since elderly patients may develop cerebral anemia and may faint in prolonged warm baths, they should be watched constantly. Unlike potassium permanganate, Dalibour's powder does not permanently stain the tub or skin. Patients who have taken both permanganate and Dalibour baths strongly prefer the latter.

It must not be thought that Dalibour's solution is a panacea for skin diseases. It has proved of no value in deep-seated pustular follicular diseases, such as acne vulgaris, sycosis vulgaris and furunculosis. Solutions of aluminum acetate and silver nitrate have proved better therapeutic agents where astringency is primarily desired, as in non-infected dermatitis venenata, eczema and so forth. Despite these shortcomings, however, Dalibour's water and its many possible modifications are valuable therapeutic agents and deserve more widespread use.

520 Commonwealth Avenue

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"DRY ICE" BURN OF THE HYPOPHARYNX

REPORT OF A CASE

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THE following case of a burn of the hypopharynx is reported because of its unusual

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etiology. "Dry ice" (solid carbon dioxide) is a caustic agent, to be classed with lye, in that it may be as dangerous as the latter when it attacks the mucous membranes, particularly in the airway and esophagus. Two similar cases were found in the literature.^{1,2} In the first one, tracheotomy was performed, whereas in the second one, as in the case reported below, the patient recovered without serious complications.

CASE REPORT

W. H., an 11-year-old boy, was admitted to the Faulkner Hospital on May 31, 1942, within 30 minutes after swallowing a teaspoonful of "dry ice" in an effort to imitate his elders smoking. Marked vomiting and expulsion of most of the "dry ice" followed promptly, but considerable difficulty in swallowing and some labored respiration persisted.

Examination of the mouth was negative. There was marked edema of the base of the tongue, hypopharynx and arytenoid cartilages. The vocal cords were normal, and respiration was adequate.

Treatment consisted of absolute bed rest. One teaspoonful of albolene was given by mouth every 4 hours. The taking of food and water by mouth was stopped. Frequent mouth washes with dilute Dobell's solution were given. The patient was closely watched, and a tracheotomy set was kept at hand in case of continued edema of the larynx.

Subsequent progress was satisfactory and the edema subsided within 4 days. Since there was considerable secondary infection, a culture showing hemolytic streptococci, with some elevation of temperature, 1 gm. of sulfadiazine was given every 4 hours, beginning on the 3rd day. After a blood level of 4.0 mg. per 100 cc. had been obtained, the dose was reduced to 0.5 gm. three times a day for 2 days, and then stopped. The patient was discharged June 7 with the temperature normal; he was able to swallow small amounts of fluids with comfort.

Two weeks after the onset, x-ray and fluoroscopic examination of the esophagus showed only a possible delay in swallowing. Since the patient was eating strained vegetables and soft solids with no discomfort, no further examination of the esophagus was made. Indirect laryngeal examination 3 weeks after the onset was negative. The patient felt well, had returned to school, and was eating as usual. Fluoroscopic and film x-ray examinations 3 months after the accident showed no deviation from normal.

270 Commonwealth Avenue

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MEDICAL PROGRESS

CHEMICAL FACTORS IN INFLAMMATION AND CELLULAR INJURY*

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OWING to limitations of time, the following discussion will be confined to certain aspects of recent studies on inflammation in this laboratory. The subjects to be dealt with are the concept of increased capillary permeability and the mechanism involved, which has led to the identification of leukotaxine in inflammatory exudates; the studies on the isolation of the leukocytosis-promoting factor; some chemical factors that condition the cellular picture in inflammation; and a brief review of the latest studies on the factor concerned in explaining the basic pattern of cellular injury in inflammation, which has led to the view that the stereopattern reaction of injury in inflammation is referable to the liberation of necrosin.

Inflammation is a manifestation of severe cellular injury, and as such represents the basis of all infectious processes. It can be readily defined as the complex vascular, lymphatic and tissue response on the part of vertebrate tissue to the presence of an irritant.^{1‡} An irritant may be considered to be any agent that interrupts normal cellular metabolism. It may be physical in nature, chemical or viable, as in the case of micro-organisms.²

Inflammation consists of a number of interdependent sequences that lead to the localization and ultimate disposal of the irritant. These phases are often grouped under the somewhat loose term "inflammatory reaction." Initially, there is a disturbance in fluid exchange, manifested by an alteration in the normal equilibrium of capillary filtration. There is at first, as shown by Landis,³ a transitory increase in capillary pressure, and this is followed by more permanent changes in the structure of the endothelial wall structure—namely, augmentation in its permeability.⁴ The enhancement in permeability can be readily demonstrated by introducing trypan blue into the circulating blood of a rabbit. The area of injury is rapidly stained blue owing to the outward passage

of the dye.⁵ The magnitude of increase in permeability is such as to allow particulated material to pass into the extra-capillary spaces.⁵ The extent of increased capillary permeability is subject to measurement. A number of years ago it was shown that, on introducing a dye into the ventricle of a pithed frog with its mesenteric capillaries exposed on the stage of a microscope,—one could evaluate with an appropriate scale the rate of change of concentration of the dye as it passes out into the extra-capillary spaces.⁶ It was found that with inflammation caused by certain irritants the permeability of capillaries is enhanced about twofold.

LEUKOTAXINE AND THE MECHANISM OF INCREASED CAPILLARY PERMEABILITY

The mechanism of increased capillary permeability in inflammation is an important factor, for it is the pivotal reaction on which all subsequent sequences depend. Lewis⁷ about twenty years ago, stimulated by the work of Ebbecke, postulated that the phenomenon is referable to the liberation of histamine or at least to a substance so closely allied to it that he termed it the "H-substance."⁷ The argument utilized by Lewis is fraught with difficulty, for it is largely one of analogy. For this reason the whole problem was reinvestigated several years ago in this laboratory. It was readily shown that the exudative fluid recovered from the site of inflammation contains a factor in turn capable of eliciting an increase in capillary permeability.⁸ This could be readily demonstrated by the seepage of a dye from the circulation into an area of skin previously inoculated with a sample of exudative material. Subsequently, chemical extraction was undertaken by first eliminating the protein fraction of exudates by treatment with pyridine and acetone. The acetone supernatant phase after desiccation is treated with butyl alcohol. The active material when kept at a low temperature comes down in the butyl alcohol phase after concentrating the latter. The material usually appears in the form of doubly refractive aggregates that at times and with proper desiccation from an aqueous medium appear in the form of needle crystals.⁹ This powerful substance, capable

*The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas, 1942, \$5.00).

†From the Department of Pathology, Harvard Medical School. Presented at the Gibson Island Conference of the American Association for the Advancement of Science, August 3, 1943.

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The references cited herein pertain primarily to the various studies of the writer. A more complete bibliography appears elsewhere.²

of inducing an increase in capillary permeability in a dilution of 1:100,000, or even in greater dilution, has been termed "leukotaxine." It is evidently not a protein. It has an α -amino group and an indole nucleus. There is evidence that it is a polypeptide to which a prosthetic group may be attached.

Leukotaxine readily diffuses out of a cellophane tube. It has none of the properties of histamine, thereby throwing considerable doubt on the view of Lewis that H-substance is primarily concerned in the mechanism of increased capillary permeability in inflammation. The whole exudate elicits the capillary reaction. Laborious extraction yields a crystalline-like substance that reproduces exactly a pattern similar to that caused by the untreated exudate. Yet the substance has none of the properties of histamine. This to a large extent invalidates the Lewis hypothesis. Leukotaxine, in contrast to histamine, fails to contract the isolated segment of guinea-pig intestine.⁹ Extracting leukotaxine for the possible presence of histamine by the method of Barsoum and Gaddum¹⁰ fails to yield any evidence that the latter is present.¹¹ Leukotaxine fails to depress the blood pressure in a cat, in contrast to the marked depressant effect of histamine.¹² It is evidently not histamine, or acetylcholine, since it fails to lower blood pressure. The following test indicates that it is probably not an adenylic compound. Parnas and Ostern¹³ have reported that adenosine induces heart block in the frog. Leukotaxine completely fails to induce any such arrhythmia.¹² Leukotaxine can evidently induce an increase in the permeability of cells in general, even among lower invertebrates. This is of significance, for it indicates the wide biologic value of this substance. For instance, it increases by about 50 per cent the permeability of the ova of the sea urchin (*Arbacia punctulata*) to sea water. This superficial effect doubtless induces a minor degree of cellular injury, for the fertilization of such eggs is followed by a retardation in cleavage development, together with atypical cleavage.¹⁴ In such ova the fertilization membrane is closely adherent to the cell, and numerous sperms are firmly attached to the membrane.

The increase in capillary permeability induced by leukotaxine has been found to be counteracted by only one substance—namely, the extract of the adrenal cortex—and to a certain extent by some of the steroid compounds derived from the adrenal cortex.¹⁵⁻¹⁷

Leukotaxine is concerned with another fundamental manifestation in inflammation—the migration of polymorphonuclear leukocytes to the site of injury.¹⁸ This is often referred to as chemotaxis. The ideas of Abramson¹⁹ on the subject, al-

though perhaps attractive as such, have unfortunately received little experimental support, either in his hands or in those of other investigators. The conclusions are primarily unsupported assumptions. The views of this worker consist in assuming that negatively charged leukocytes in an electronegative blood stream readily migrate, as in a cataphoretic chamber, into a positively charged area of connective tissue that has previously been injured. Leukotaxine does not as yet explain the exact intrinsic cellular mechanism concerned in the motion of leukocytes, but it at least stands out as a concrete substance, liberated in exudates, that is definitely chemotactic. This fact in itself offers the distinct possibility of attacking the problem further in an endeavor to determine how leukotaxine specifically affects the mobility of white cells so as to induce their migration to the site of inflammation. Whether electric charges have anything to do with the phenomenon remains to be proved. The end product of blood serum extracted for leukotaxine yields no activity so far as cell migration is concerned. On the other hand, leukotaxine derived from exudates is definitely chemotactic, for its injection into tissues induces not only a marked increase in capillary permeability but also a distinct migration of polymorphonuclear cells outward into the area of injury. The chemotactic property of leukotaxine can be easily demonstrated by in vitro observations.² The placing of leukotaxine crystals on a slide containing a drop of exudate is soon followed by migration and clustering of cells at the periphery of particles of leukotaxine. No such effect is observed with either carbon particles or reduced iron powder.

In conclusion, leukotaxine extracted from inflammatory exudates offers a reasonable explanation for two of the basic sequences in inflammation—namely, the mechanism of increased capillary permeability and the local migration of polymorphonuclear leukocytes. Besides these two functions, leukotaxine appears to be relatively innocuous so far as the induction of any appreciable tissue injury is concerned.

THE MECHANISM OF LEUKOCYTOSIS WITH INFLAMMATION

The leukocytosis-promoting factor is another potent biologic substance recently isolated from the site of inflammation. Leukotaxine introduced into the circulating blood fails to alter the number of white cells.²⁰ Yet it is well known that in numerous inflammatory processes the level of circulating leukocytes is considerably elevated. The leukocytosis has been shown to be referable to a chemical unit.²⁰ The injection of whole exudative material into the blood stream of a dog induces a prompt leukocytic response. Neither leukotaxine nor blood

serum is capable of eliciting such a reaction. The evidence indicates that there is a leukocytosis-promoting factor present in inflammatory exudates. This factor in contrast to leukotaxine is nondiffusible, and it is thermolabile.²⁰ Its injection is accompanied by a discharge of immature leukocytes into the circulation. Chemical extraction of exudates

anism of leukocytosis accompanying numerous inflammatory processes. Its marked growth effect on some of the elements of the bone marrow obviously may prove to have clinical implications. These require no further comment.

CYTOLOGIC SEQUENCE IN INFLAMMATION

Another fundamental sequence in the development of the inflammatory reaction is the initial infiltration of polymorphonuclear leukocytes, which are subsequently replaced by macrophages. This is an almost invariable cytologic sequence.²⁷⁻²⁹ With some irritants the polymorphonuclear phase may be lengthened and the macrophage one correspondingly shortened—for example, staphylococcal abscess—or vice versa—for example, the tubercle. Nevertheless, the same basic principle is maintained. Several years ago it was observed

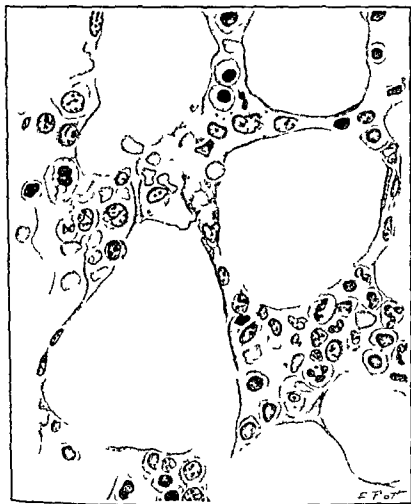


FIGURE 1.

This drawing of a section through the femoral bone marrow of a dog that had received several days previously an injection of the pseudoglobulin fraction derived from normal blood serum shows that the marrow is essentially normal.

yields activity in the pseudoglobulin fraction.²¹ Other protein fractions such as albumin and euglobulin are ineffective in inducing a state of leukocytosis. The material is absent in normal blood serum, but can be recovered from the serum of an animal with a concomitant inflammation.²² This fact suggests that it reaches the bone marrow by way of the blood stream. The material can be obtained from the exudates of dogs and rabbits^{2 23} and of human beings.²⁴

The most recent finding in connection with the leukocytosis-promoting factor is its capacity not only to discharge immature granulocytes into the circulation but also to induce a marked and specific growth effect in the bone marrow.^{25, 26} The result is a conspicuous hyperplasia of some of the hematopoietic elements, notably the granulocytes and the megakaryocytes (Figs. 1 and 2).

In brief, the leukocytosis-promoting factor of exudates offers a reasonable explanation for the mech-

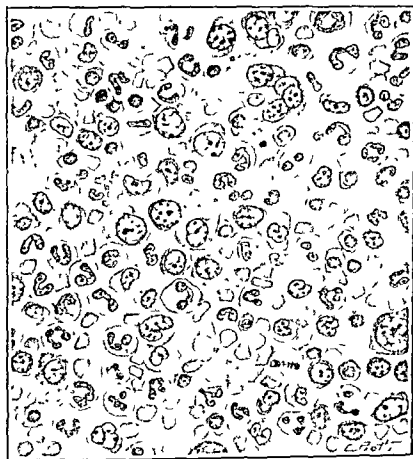


FIGURE 2.

This drawing of a section through the femoral bone marrow of a dog that had received several days previously an injection of 87 mg. of leukocytosis-promoting factor derived from exudative material shows an extensive hyperplastic response replacing the usual areas of adiposity. A mitotic figure is in evidence. The factor seems to stimulate primarily the growth of granulocytic elements and of megakaryocytes.

that this phenomenon is referable to a developing local acidosis at the site of an acute inflammation.³⁰ In earlier studies it was demonstrated that the local circulation in an inflamed area is markedly impaired.³¹ The lymphatic outlets become occluded, and in time thrombi are also found in

the smaller vascular channels. Thus, the area of inflammation becomes, so to speak, shunted from the rest of the organism. It develops its own hydrogen-ion concentration, its own circulation and its own metabolism. The polymorphonuclear leukocytes brought to the site of injury through the action of leukotaxine, as described above, are unable to survive below pH 7.0, whereas the mononuclear phagocytes appear fairly normal at pH 6.9 to 6.8. At a somewhat lower pH all types of leukocytes tend to be injured. The result is a state of suppuration. Pus is virtually a function of the hydrogen-ion concentration. For instance, a twenty-four-hour exudate from the pleural cavity of a dog previously injected with turpentine is primarily composed of polymorphonuclear leukocytes, whereas an exudate of several days' duration at pH 6.5 reveals an absence of normal polymorphonuclear cells. The rise in hydrogen-ion concentration tends to precede the change in the differential leukocyte picture. On the other hand, if the reaction remains alkaline during the development of the inflammatory reaction, the cellular picture is characterized throughout by a predominance of polymorphonuclear leukocytes. That the general effect is an inability on the part of polymorphonuclear leukocytes to survive at an acid reaction has been demonstrated by subjecting leukocytes in vitro to buffers at various hydrogen-ion concentrations.³² In this way it is readily shown that these cells tend to cluster and become swollen with coarse granulation at about pH 6.5. When supravitality stained, the nuclei take up the dye, indicating severe injury. These changes are absent in cells exposed to pH 7.4.

It is of importance to determine the mechanism of local acidosis with inflammation if one is to comprehend the forces at work in conditioning the cytologic picture at the site of an acute inflammation. The alkali reserve of the exudate tends to decrease with the developing local acidosis.³³ This in itself might be expected to occur, for it is another means of expressing the rise in hydrogen-ion concentration. Incidentally, it is well to emphasize again that all the biochemical changes are local; the reaction of the blood remains essentially unaltered.

The local acidosis seems to be primarily referable to a glycolytic process.³³ The result is a true lactic acid acidosis. Several chemical variables have been studied in the exudate during the progress of the inflammatory reaction. These include the concentration of sugar and of lactic acid and the measurement of the pH, correlated in turn with the cellular picture. The conversion of glucose to lactic acid induces a local acidosis,

with the resulting effect on the leukocytes described above.

In conclusion, the cellular picture in inflammation is primarily conditioned by the hydrogen-ion concentration, which in turn seems to be referable to a disturbance in the intermediary carbohydrate metabolism. The lymphocytes appear to be unaffected—at least directly—by the changes in hydrogen-ion concentration. The function of the latter cells is still somewhat obscure. The studies of McMaster and Hudack³⁴ and the more recent work of Ehrlich and Harris³⁵ suggest their possible role in the formation of antibodies.

DIABETES AND INFLAMMATION

The biochemical studies on the relation of hydrogen-ion concentration to the cellular picture at the site of an acute inflammation have led to further extensive investigation in an attempt to unravel the mechanism concerned in the intensifying of the diabetic state when there is a superimposed inflammation in depancreatized dogs.³⁶ Time forbids discussion of the details of this work. Suffice it to say that an inflamed area is a focus of proteolysis. At the site of inflammation in a diabetic animal the breakdown of proteins is considerably exaggerated. Local gluconeogenesis from the deaminated part of the protein molecule readily explains the heightening in blood sugar following the diffusion of glucose previously formed at the site of injury. Close analysis indicates that in general, even in nondiabetic animals, glucose is capable of being formed by injured cells.³⁷ Such cells are therefore potentially foci of gluconeogenesis. The process is merely exaggerated in the diabetic animal. There is also some additional evidence that urea, besides originating in the liver, is likewise formed at the site of an acute inflammation.³⁷

THE CHEMICAL BASIS OF INJURY IN INFLAMMATION

The last phase of the most recent studies to be considered here is the presence of a fundamentally stereopattern of injury in the development of the inflammatory reaction, irrespective of the irritant. The latter and the anatomic location of the lesion may modify its ultimate appearance. Nevertheless, close scrutiny reveals a basic pattern of injury. For instance, damaged cells may show granular elements strewn through their cytoplasm; the cells may be vacuolated; the collagenous bundles may appear swollen; and the nuclei may reveal various degrees of pyknosis. Another evidence of tissue injury found in a variety of acute inflammatory lesions is displayed by the fibrinous occlusion of lymph

phatics and also by the presence of small thrombi in the blood vessels of an inflamed area.¹

It may be asked whether the mechanism that accounts for the basic pattern of injury in inflammation is referable to a chemical unit. Leukotaxine scarcely induces any degree of injury to cells except for an augmentation of cellular permeability. The leukocytosis-promoting factor elicits essentially no injury to tissues. Recent studies, however, have indicated that the euglobulin fraction of exudates is highly injurious to the cutaneous structures of the rabbit and to some extent to those of the dog.³⁸ There is thus an accumulated body of evidence that either in the euglobulin fraction of exudates or else associated with it there is present an injury factor capable per se of reproducing the nocuous effects seen in inflammation. This substance or factor has for the sake of convenience been termed "necrosin."³⁸ Its injection into the skin of rabbits is accompanied by intense redness, edema and usually a central area of necrosis. No other fractions of exudate appear to be capable of inducing any such effect. Furthermore, the euglobulin fraction of normal blood serum elicits absolutely no appreciable lesion in the skin of rabbits. On the other hand, the same fraction from the serum of a dog with a concomitant acute pleural inflammation frequently induces a severe inflammation. This observation suggests that the toxic substance is absorbed from the site of inflammation into the circulation, whence it can be recovered. This fact is perhaps of significance in re-evaluating the concept of a focus of infection and its far-reaching repercussions to other organs.

Necrosin induces an acute inflammation with blockade of the lymphatics. A section through such an area reveals zones of dense leukocytic infiltration in which the lymphatic channels may be occluded by thrombi.³⁹ Small vascular channels may also show evidence of thrombosis. On the other hand, the euglobulin fraction of normal serum leaves the lymphatic channels essentially patent. About ten minutes after the injection of necrosin into the skin of rabbits the collagen bundles often appear to be swollen, with a tendency to fuse together. The latter seems to be one of the first morphologic evidences of the injurious effect of necrosin on supporting structures.

As stated previously, necrosin can be recovered from the blood serum of an animal with an acute inflammation. This interesting observation, which may reasonably explain the toxic effect of a lesion on organs at a distance, has suggested the necessity of examining the generalized effect on organs of an intravenous injection of necrosin.³⁹ Although several organs, such as the gastrointestinal tract, may show evidence of injury, or various lymphoid structure may reveal signs of enlargement and

congestion, it is nevertheless only the liver and to some extent the kidneys that seem most frequently to exemplify signs of damage. Many of the parenchymatous cells of the liver appear swollen and contain many fat vacuoles. There are interspersed foci of leukocytic infiltration, reminiscent of hepatic focal necrosis. The liver on gross examination is streaked with what seems to be yellowish or whitish foci. In some cases the cell outlines have disappeared and the liver cords are stippled with coarse, black-stained granules that do not take the iron stain. The epithelial lining of the kidney tubules may show irregularities and vacuolation, and foci of leukocytic infiltration separating some of the tubular structures may also be present.

Various investigators^{40, 41} who have studied the problem of traumatic or surgical shock have arrived at the conclusion that one or several toxic substances are absorbed into the circulation from the site of acute injury. It is indeed quite conceivable that in the syndrome of shock there are several such substances, and furthermore that the clinical picture of shock is to a large extent due to some of these substances in addition to superimposed systemic neurologic factors and to an alteration in the blood volume. At any rate, necrosin per se fails to depress the blood pressure in a cat, in contrast to the action of histamine.³⁹ It is quite conceivable that in shock the fall in vascular tension is referable to histamine, whereas the other noxious effects are due in part to the liberation of necrosin at the site of injury.

There are two additional properties of necrosin that indicate its significance to the student of pathology. Its intravenous injection into a dog is accompanied by severe toxic manifestations, including vomiting and diarrhea. For a while the animal lies on its side and appears somewhat prostrated. Of greater significance is the abrupt fall in the number of circulating leukocytes, which is usually extremely marked. The white-cell count may fall in an hour or two from about 10,000 to 1000 or 2000. After several hours the dog appears to be clinically improved and the white-cell count rises. Subsequently or on the following day a leukocytosis may ensue. It is conceivable that the latter is a secondary effect caused by the initial injury of various organs by necrosin, which thus allows the release of the leukocytosis-promoting factor. The inability of other fractions of exudate to induce leukopenia suggests that the liberation of necrosin at the site of injury and its absorption into the blood stream are actively concerned in the mechanism of the developing leukopenia accompanying certain infectious processes.

Of perhaps even greater interest is the fact that the intravenous injection of necrosin in dogs is accompanied by a marked rise in temperature simul-

taneous with the developing leukopenia, possibly of 3 to 5°F. The early studies of Grafe⁴² suggested that in infectious processes the fever is referable to the absorption of products of cellular disintegration. Other protein fractions of exudate—for example, the leukocytosis-promoting factor or the euglobulin fraction of normal serum or of ascitic fluid—are all incapable of inducing any fever when injected into the circulating blood of a dog. The fact that necrosin seems to be the only fraction to have this capacity suggests strongly its possible role in the production of fever with inflammation.³⁹

SUMMARY AND CONCLUSIONS

The presence of leukotaxine, the leukocytosis-promoting factor and necrosin in inflammatory exudates offers a reasonable explanation for the development of a fundamental pattern in inflammation. Observations suggest that an irritant irrespective of its nature severely injures cells, which in turn, as a result of their deranged metabolism, liberate various common denominators—for example, leukotaxine, the leukocytosis-promoting factor and necrosin. These substances, which are to be regarded as constant products of marked cellular injury, are responsible for the recognized pattern of the inflammatory reaction.

The salient sequences in inflammation besides the basic injury caused by the presence of necrosin may be recapitulated as follows²:

- (1) *Disturbance in local fluid exchange.*
 - (a) Increase in capillary permeability, which is primarily referable to liberation of leukotaxine.
 - (b) Initial increase in lymph flow.
- (2) *Localization of the irritant (fixation).*

Time has prevented any discussion of this earlier work, which has led to the view that inflammation is the regulator of bacterial invasiveness through its ability to induce blockade¹ of the lymphatics. Thus, the dissemination of a micro-organism bears in large part an inverse function to the induced degree of local injury and a direct function to time.
- (3) *Migration of leukocytes.*
 - (a) The diapedesis of polymorphonuclear leukocytes is referable to the liberation of leukotaxine.
 - (b) The cytologic sequence at the site of an acute inflammation is conditioned by the local hydrogen-ion concentration.

- (c) The leukocytosis in the circulating blood stream is referable to the liberation at the site of inflammation of a pseudoglobulin, the leukocytosis-promoting factor.

The interplay of the foregoing sequences favors the localization and the ultimate disposal of the irritant. This leads to the final reparative phase of the injured area. There are suggestive observations that repair may also be due to the liberation of growth-promoting factors by mildly injured cells.⁴³ Necrosin seems to be released by the cell that is severely injured by an irritant, and thus the appearance of necrosin initiates the inflammatory process. Its chemical separation from the rest of the exudative fluid becomes a necessity in any endeavor to determine whether proliferative or reparative factors derived from probably less severely injured cells are likewise present in exudates. Such studies are now under way.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 29381

PRESENTATION OF CASE

A fifty-one-year-old man, a factory worker, entered the hospital because of acute abdominal pain.

One week prior to admission the patient developed upper abdominal "distress," the nature of which he was not able to describe well. It was apparently not related to food. There was no associated back or shoulder pain, nausea or vomiting, but he was forced to stop working. His bowel movements had been fairly normal with a laxative prescribed by his physician. At the onset of his present illness he contracted a "cold" after removing storm windows. There were no chills, fever, urinary disturbances or chest pain. He had remained in bed more or less constantly. On the night before admission the pain in the abdomen became worse and he developed chilly sensations. He was given a hypodermic by his doctor and sent into the hospital. There was no vomiting. His last bowel movement had been two days before admission, at which time he had two loose stools. He had not passed gas by rectum since then.

Physical examination disclosed a moderately obese man with questionable cyanosis of the lips and fingernails. The skin was moist. The heart was not enlarged. A short systolic murmur was heard in the aortic region, which was not transmitted. The aortic second sound was greater than the pulmonic. The heart rate was regular and of good quality. The lungs were clear. The abdomen was flat. No peristalsis could be detected anywhere. There was voluntary spasm all over, but when the muscles were relaxed by flexion of the legs, there was variable response to palpation — once it was "sore," then "no pain," then "a little tender" and so on. No definite masses were felt. There was no costovertebral tenderness. Rectal examination showed no tenderness or masses. The prostate was slightly enlarged. There was no edema or ascites.

*On leave of absence.

The blood pressure was 158 systolic, 80 diastolic. The temperature, pulse and respirations were not recorded.

Urine examination was negative. Examination of the blood showed a white-cell count of 16,200, with 84 per cent neutrophils. Three hours later the white-cell count was 11,300. A blood Hinton test was negative. An electrocardiogram was interpreted as showing normal rhythm, at a rate of 80, with low T₂ and total inversion of Lead 3; Lead 4 was normal.

A roentgenogram of the abdomen showed considerable gas and fecal material in the proximal colon. The colon distal to the splenic flexure was collapsed. A film taken on the following day in the prone and upright positions showed several dilated loops of small bowel on both sides of the midabdomen as well as a large, single loop of bowel that appeared to be small intestine. There was also a small amount of gas in the colon in the region of the splenic flexure. An upright film showed fluid levels within several of the loops on the right side of the abdomen. There was no air beneath the diaphragm. A barium enema on the second hospital day revealed the passage of barium to the cecum and the terminal ileum without delay. There was a moderate amount of fecal material within the colon that somewhat hindered the examination. No gross evidence of obstruction or definite evidence of ulceration or of a filling defect could be seen. There were two loops of slightly dilated air-filled small bowel in the left midabdomen. Barium passed through the ileum to the air-filled loops of bowel, and one loop gave the appearance of partially encircling a mass over the left side of the lumbosacral junction; the loop in question was somewhat narrowed and irregular in outline.

An electrocardiogram on the third hospital day was normal.

On the third hospital day the patient had a spontaneous bowel movement. Peristalsis was audible, and the abdomen flat. On further questioning it was brought out that the patient had had two former episodes of substernal pressure with radiation down the left arm, lasting three to five minutes and coming on while he was working on a chair. These attacks had been diagnosed as angina pectoris and the patient was advised to live a moderately restricted life. Since then the patient had had no similar episodes.

A gastrointestinal series on the fifth hospital day showed that the passage of barium through the pylorus was very slow. A large residue of barium was seen in the colon, especially in the region of the cecum, which was dilated. There was considerable gas in the hepatic and splenic flexures. Hourly films showed slow passage of

barium to the small bowel, and for a period of three hours no progression was seen. The stomach was almost completely empty at three hours, and all the barium was found to be in a few loops of small intestine on the left side of the abdomen in the region where the air filled loops were visible on the previous examination. At four hours, however, barium had passed through the narrowed loops previously described. Spot films taken over this region showed no definite evidence of ulceration. The narrowing was believed to have been due to extrinsic pressure. At four hours the head of the barium meal was in the region of the ileocecal valve, but had not entered the cecum. No mass could be definitely visualized.

Following the gastrointestinal series the patient was given an enema, with good results. He was seen twice that evening and appeared well. At about 4:00 the following morning he began to complain of gas pains, and another enema was given. Soon after that the patient was found to be sweating profusely. The blood pressure could not be obtained. The abdomen was slightly distended. The pulse was about 120. Examination of the blood revealed a white cell count of 29,800, with 87 per cent neutrophils. Intravenous fluids were given, and a Miller-Abbott tube inserted. The patient's condition apparently improved throughout the day. The following night he passed 50 cc of bright red blood.

The white cell count on the seventh hospital day was 22,300, with 91 per cent neutrophils. The urine showed a ++ test for albumin. The non-protein nitrogen was 44 mg per 100 cc, the protein 58 gm. The chloride was 928 milliequiv per liter, the carbon dioxide combining power 20.6 millimols. The serum amylase was normal. A portable film of the abdomen showed no demonstrable air filled small intestine. The stomach was filled with air, and the colon contained a large amount of barium and considerable gas.

A film taken on the eighth day showed the tip of the Miller-Abbott tube in the second portion of the duodenum. There appeared to be a small amount of gas in the slightly dilated bowel. A large amount of barium was seen in the large intestine. The right side of the diaphragm was elevated, and there were linear areas of atelectasis in the right lower lung field. The abdomen remained somewhat distended. The Miller-Abbott tube was passed to the jejunum, as confirmed by x-ray, and the stomach was kept decompressed by a Levine tube.

The white cell count on the eleventh hospital day was 31,300, the hemoglobin 12.6 gm. The blood protein was 6.0 gm per 100 cc, and the chloride 97.2 milliequiv per liter. A portable film now

showed considerable air in the stomach and some gas filled bowel, presumably the colon. The Miller-Abbott tube lay over the lumbosacral articulation.

The following day the patient passed dark blood by rectum and had some bloody drainage through the Miller-Abbott tube. He became pulseless, comatose and died.

DIFFERENTIAL DIAGNOSIS

DR CARROLL C MILLER. This case seems to be covered with mystery and confusion concerning several of its details. A large part of the discussion concerns itself with the x-ray findings, none of these prove anything, and so far as I can figure out they do not help particularly in making a diagnosis. There are two points that we must ascertain in diagnosing such a problem: the location of the trouble and whether it is intrinsic or extrinsic in relation to the gastrointestinal tract. If it is intrinsic, is it an infectious condition or is it a vascular disturbance? If it is extrinsic, has it ulcerated into the bowel so as to provide us with an explanation of the symptoms and signs? We should like to know about the presence of abdominal tenderness and pain. The temperature is not recorded. The pulse was essentially normal when the patient first came in, but after the shocklike episode on the sixth day the pulse rose to 120. According to the chart before us, five or six days after admission the temperature rose from the normal to 101°F by rectum and stayed more or less at that level without any appreciable change. There was a concomitant rise in pulse and respirations. So we do not have a definite picture of a rising curve or of an intermittent spiking one. We do not know what the hemoglobin was when the patient was first seen, so that we have no way of comparing the last note of 12.6 gm with the former condition.

Since so much space in the abstract has been given to discussion of the x-ray films it might be interesting to see them now.

DR LAURENCE L. ROBBINS. These films are arranged more or less according to the time relation in which they were taken. I have left out those that are not particularly pertinent. It might be said that perhaps the diagnosis should have been made by x-ray. I am not at all sure about that, however.

This is the appearance at the time the patient entered the hospital, with a large amount of fecal material on the right side of the colon. The next day, probably after enemas, we notice that the colon is fairly well cleared out and that there is this air filled small bowel. The following day a barium enema was given, and the colon is apparently normal. These are the loops of small bowel that

were described as air containing, and you notice that the barium passes up to a point close to the air-filled loops. This loop of ileum appears to go around something (Fig. 1). In the same area

DR. MILLER: How far away from the ileocecal valve would you say this was?

DR. ROBBINS: About 75 cm. An exceptionally large amount of Larium passed into the small



FIGURE 1. X-Ray Film following a Barium Enema.

The abnormal loop of ileum appears to be partially surrounding a mass over the left side of the lumbosacral junction.

you see another loop of ileum that appears to overlie the questionable mass. This loop of bowel is definitely abnormal, I should say. So far as one can tell it is small and probably has some mucosal swelling. I cannot see anything that indicates a definite ulcer. Later films of the small bowel more or less confirm these findings except that there is nothing on which one can make a positive diagnosis of a mass at this time, and the suggestion of the loop of bowel constantly going around something is lost (Fig. 2). In this area, however, the mucosa again appears abnormal and that is confirmed by this spot film. I have seen a similar appearance in the mucosa of the sigmoid in a case of periarteritis nodosa. I am not trying to lead anyone astray, but that is the only similarity I have seen.

bowel. I think you can be sure there is definite abnormality of the mucosa of the ileum.

DR. MILLER: Because of the repeatedly high white-cell count and the high percentage of neutrophils, we must assume that something fairly acute in the way of either sepsis or necrosis was going on, and because of a variation during the investigation, at times distention and at times collapse of the bowel, and also because of the terminal episode of hemorrhage into the intestine, we must presuppose that something was going on intraluminally, which allowed blood to escape into the bowel. It will be hard to make a diagnosis that satisfies both these conditions.

There are several things to think of, but we do not have enough evidence to rule them entirely in or out. A sigmoidal diverticulitis with abscess

and rupture might account for localized peritonitis and for subsequent bleeding from the bowel. A mesenteric thrombosis would account for the signs of necrosis in the small intestine, accompanied by

hemorrhage coming from a mesenteric thrombosis or an internal hernia with strangulation.

The mass that this loop of bowel encircles might be either abscess or retroperitoneal tumor. It is



FIGURE 2. X-Ray Film following a Barium Meal.

The abnormality of the loop of ileum is still visible, but the apparent mass has disappeared.

a high white-cell count and some degree of fever. The chart is possibly consistent with that. It would also account for the terminal bleeding episode. It is not likely that this condition is malignant disease. In the first place, there was no previous history. The man was in reasonably good condition; in fact he was described as being somewhat obese. No masses were felt. However, acute abdominal emergencies are sometimes simulated by extensive metastatic lymph-node involvement in the abdomen because of sudden spread or rupture.

An internal hernia with strangulation of a loop of bowel might account for intermittent obstruction and eventual necrosis of that segment of the bowel, with intraluminal bleeding. I should like to think of the terminal episode as being due to

not likely that any retroperitoneal tumor would also so involve the small intestine as to produce this picture. An abscess can involve the wall of the bowel causing obstruction and bleeding, although it is not likely.

A condition that we often forget but which occurs fairly frequently is a Meckel's diverticulitis. In a Meckel's diverticulum there may be bleeding from a peptic ulcer, and it may also become infected, with rupture. From the x-ray picture it is possible that an abscess had formed around a diverticulum of the small intestine and that the loop of bowel had become involved in that area; there might still have been a communication into the lumen of the bowel to account for bleeding by rectum and by the Miller-Abbott tube.

I think we must postulate an infectious process

in the form of an abscess, with involvement of a loop of small bowel. I think as a best bet I shall say that this patient had a Meckel's diverticulum or a diverticulum of the sigmoid—a solitary one that was not seen by x-ray—accompanied by abscess and hemorrhage through erosion of a large mesenteric vessel.

DR. ROBBINS: I am not at all sure I made myself clear to you, Dr. Miller. The small-bowel studies do not confirm the presence of the mass suggested by the barium enema; the films are not characteristic of bowel going around a mass.

DR. MILLER: Nevertheless, there is a loop that is abnormal, either by distortion or extrinsic pressure.

DR. ROBBINS: It may be intrinsic disease.

DR. MILLER: Of course, a localized regional enteritis is possible, although it is not commonly seen so far back in the ileum as this. Furthermore, I do not believe that in cases of terminal or regional ileitis one often observes a terminal episode such as this patient had, with almost no cachexia or general disturbance.

DR. EDWARD B. BENEDICT: I do not see why this would not go with regional enteritis.

DR. ROBBINS: Would one have acute episodes with it?

DR. BENEDICT: No.

DR. MILLER: One does not as a rule see such a massive lesion as this man had. Furthermore, such patients are usually younger.

DR. RICHARD H. SWEET: As Dr. Miller clearly brought out, I believe there must have been some necrosis of the loop of bowel to explain this picture.

CLINICAL DIAGNOSES

Small-bowel obstruction.

Volvulus?

Intussusception?

DR. MILLER'S DIAGNOSIS

Meckel's or sigmoidal diverticulitis, accompanied by abscess and hemorrhage.

ANATOMICAL DIAGNOSES

Mesenteric venous thrombosis.

Infarction of small intestine.

Hemorrhage into intestinal tract.

Peritonitis, acute, fibrinous.

Hemoperitoneum.

Coronary thrombosis, old.

Arteriosclerosis, marked, generalized.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: At the autopsy we found 3000 cc. of hemorrhagic fibrinous fluid and

blood in the abdomen. The entire jejunum and most of the ileum, to within about 150 cm. (6 feet) of the ileocecal valve were covered with bluish fibrin. Parts of the bowel were obviously gangrenous, and other parts showed beginning infarction. The cause of this gangrene was a mesenteric venous thrombosis. The arteries and arterioles were uninvolved. There was no periarteritis nodosa. The entire intestinal tract was filled with old and recent blood, apparently arising from the massive necrosis of the small bowel, which had terminally perforated into the abdominal cavity.

Most of the cases of mesenteric occlusion that we see are arterial in type and are caused by emboli. The venous type is uncommon and little is known about its etiology. In contrast to the arterial it does not usually come on suddenly with severe abdominal pain.

DR. ROBBINS: Could you find evidence of old infarction?

DR. CASTLEMAN: The thrombi were of various ages, and in some there was definite organization.

The patient also had an old thrombosis of the left descending coronary artery, which accounted for the anginal attacks.

CASE 29382

PRESENTATION OF CASE

A fifty-two-year-old man entered the hospital because of severe pain under the xiphoid.

Five years prior to admission the patient suffered his first attack of sharp upper abdominal, midline pain that lasted four or five hours. He entered a community hospital, where extensive studies were done and reported to be negative. He was discharged after two weeks.

Four years and three years prior to admission he had similar attacks of epigastric pain that radiated to both shoulders and to the upper anterior chest. These lasted six and fourteen hours and spontaneously cleared. Seven weeks prior to admission he re-entered the same hospital because of an attack of pain, but since repeated studies were again negative he was promptly discharged. He continued to have these attacks, and six days prior to admission he collapsed during one of them. These episodes had no relation to meals. At times he found that milk and doughnuts partly relieved the pain, and for several years he had drunk 4 to 5 quarts of milk a day. During the previous three months the pain had often been relieved by induced vomiting. There was no nausea, vomiting, anorexia, fever, chills or jaundice. The stools were never tarry, bloody or clay colored. During the previous year constipation had become bothersome but had always been relieved by cathartics.

The patient had lost 15 pounds during the three months prior to admission.

The family and past histories were noncontributory.

Physical examination disclosed a 250 pound man who seemed very restless. The lungs and heart were normal. The abdomen was markedly distended and tympanitic, but peristalsis was normal. No masses were felt, and no tenderness was elicited.

The blood pressure was 110 systolic, 70 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a hemoglobin of 90 per cent, and a white-cell count of 10,200, with 77 per cent neutrophils. The urine was nor-



FIGURE 1. Portion of Film Showing an Ulcerated Lesion in the Second Portion of the Duodenum.

mal. The stool was guaiac negative on two occasions. The blood Hinton test was negative. The nonprotein nitrogen was 14 mg. per 100 cc., the protein 75 gm. per 100 cc., and the chloride 990 milliequiv. per liter. The van den Bergh reaction was normal.

A Graham test was negative. A gastrointestinal series disclosed a normal esophagus. The stomach was high and transverse in position but normal in form and function. The duodenal bulb filled to a normal contour. Just beyond the bulb, along the

posterior and lateral aspects of the second portion of the duodenum, there was an ulceration 1 by 2 cm. in size. About this area, and extending downward along the second portion of the duodenum for a distance of 7 cm., there was a rigid area of narrowing, and laterally there seemed to be a rather sharply outlined 2-by-4-cm. defect encroaching on the duodenum, in which the ulcer lay

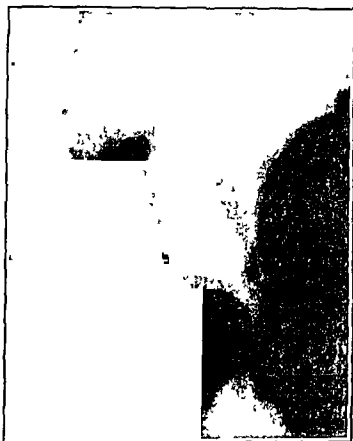


FIGURE 2. Spot Film Demonstrating the Ulcerated Lesion with Surrounding Edema.

(Figs. 1 and 2). Beyond this the duodenum was of rather unusually large caliber. There was no obstruction to the flow of barium through this area. No definite fistulous communications were observed. There were opacities along the course of the colon, probably residue of opaque material previously given.

A barium enema passed readily from the rectum to the cecum and outlined a normal large bowel.

An operation was performed on the thirteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD B. BENEDICT: Practically the only positive finding we have is that seen on the x-ray film. It seems to me that the case is either extremely simple or extremely difficult, and judging from the comments and the strange looks that the people to whom I have talked about it have given me, it looks a little complicated.

The pain radiating to both shoulders seems unusual, so I spoke to Dr. Chester M. Jones about it since he has written a book on digestive tract pain. He mentioned various possibilities. The heart, from

what I am told, will occasionally give pain radiating to both shoulders, although it is unusual. In this case the heart was entirely normal. Hiatus hernia or other disease of the esophagus with spasm may give pain radiating to both shoulders, but the esophagus was normal by x-ray. Volvulus of the stomach also gives this type of pain, but we have no evidence of that. Gallstones may do it, but the Graham test was negative. The second portion of the duodenum is a rare place for a peptic ulcer, but it may occur.

The fact that there was rigidity of the second portion of the duodenum makes one think of malignant disease in addition to a simple ulcer, but the five-year history is long for malignant disease. It is noted in the x-ray report that the ulcer was situated posteriorly and laterally. Posteriorly the second portion of the duodenum is in relation to the kidney, and it makes one think that possibly this might have been a kidney lesion; but the urine was negative and there were no other signs pointing to a kidney lesion. Laterally the right colic flexure is in relation to the second portion of the duodenum, but the barium enema was negative, which appears to rule out a lesion of the colon that might have perforated into the duodenum. Again, we have the long-standing history that makes a malignant lesion quite unlikely.

Concerning lesions of the pancreas, common bile duct and ampulla of Vater, these organs are all medial, and this lesion was lateral and posterior. Moreover, with a lesion of the pancreas, common bile duct or ampulla, one would naturally expect jaundice. This patient had not been jaundiced. A retroperitoneal lesion other than the kidney, such as sarcoma, might be considered, but the duration seems to have been too long, and I do not believe that I have ever seen one ulcerate into the duodenum.

So we come down to the possibility of simple ulcer of the second portion of the duodenum. These do occur, although they are rare, and everything in the history goes with it. I believe that a peptic ulcer of the duodenum can give pain radiating to both shoulders, which is relieved by milk and doughnuts. He had lost only 15 pounds, which is compatible with a benign peptic ulcer. The physical examination and the laboratory findings contributed nothing. The repeated area of narrowing bothers me, but I think that can go with a cicatricial stenosis associated with a duodenal ulcer. As my first diagnosis, I shall put down benign peptic ulcer of the second portion of the duodenum with cicatricial stenosis, bearing in mind that a carcinoma in that region is also a possibility.

May we now see the x-ray films?

DR. MILFORD SCHULZ: These films of the esophagus and stomach are normal and probably rule out hiatus hernia. The ulcer, which is seen to better advantage on the spot films, lies in this rather constant rounded defect in the second portion of the duodenum.

DR. BENEDICT: Where would you place the ampulla of Vater?

DR. SCHULZ: It should be lower than where the ulcer is, and more medial. This area of narrowing remains quite constant throughout the examination.

DR. BENEDICT: Do you think that it is consistent with a cicatricial stenosis? Or has it got to be a malignant lesion? Or is that not a fair question?

DR. SCHULZ: I should think that either a tumor mass or a scarring of long standing could produce this type of narrowing and constant deformity.

DR. BENEDICT: You are sure it is not medial? It could not be an ulcerating carcinoma of the pancreas?

DR. SCHULZ: No.

DR. BENEDICT: Ulceration of the pancreas is rather unusual on the opposite side of the duodenum. I cannot think of anything else. I shall stick to my original diagnosis.

DR. RICHARD H. SWEET: On a statistical basis would not carcinoma be more frequent than benign ulcer in that location?

DR. BENEDICT: I put that in as a second possibility.

DR. SWEET: I was merely going on the statistical frequency.

DR. BENEDICT: What about the five years' duration?

DR. SWEET: I do not know.

DR. JACOB LERMAN: What about an ulcerating polyp in the duodenum?

DR. SCHULZ: The lesion does not look like a polyp in the x-ray film. It may be a tumor, or it may be just edema of the duodenum.

DR. BENJAMIN CASTLEMAN: The surgeon made leiomyosarcoma of the duodenum as his preoperative diagnosis. Have you anything to say about that?

DR. BENEDICT: I do not believe that I have ever seen one. They are extremely rare.

DR. CASTLEMAN: We have had a few intramural tumors of the second and third portions of the duodenum, but they certainly are not so common as carcinoma or even as peptic ulcer.

DR. FRANCIS D. MOORE: The striking thing about the patient preoperatively was the terrific pain, which was unrelieved by ordinary measures. The diagnosis of leiomyosarcoma was a far-fetched

attempt on the part of the service to reconcile the long history with the existing lesion, with the idea that it might have been a leiomyoma for a period of years and had then undergone malignant degeneration. Dr. Leland S. McKittrick operated on the patient and found a mass in the duodenum that was the size of an orange, a great deal of it apparently being tumor with superimposed inflammatory change. There were no lymph-node or liver metastases. A Whipple operation was performed, the duodenum being removed, the gall-bladder anastomosed to the jejunum, a gastrojejunostomy performed and the end of the pancreas closed off. The specimen was opened and showed an ulcerated lesion with raised margins, which appeared to have invaded the surrounding tissue.

CLINICAL DIAGNOSIS

Leiomyosarcoma of duodenum.

DR. BENEDICT'S DIAGNOSIS

Peptic ulcer of duodenum.

ANATOMICAL DIAGNOSIS

Peptic ulcer of duodenum.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: In the gross we found, 1.5 cm. above the papilla of Vater, a sharply demarcated ulcerated lesion approximately 2.5 cm. in diameter with slightly overhanging edges. As Dr. Moore has said, there was a lot of induration around it, which extended into the surrounding fat. We cut one section through the center of the lesion for microscopic examination and found what looked like a perfectly benign peptic ulcer. Since a peptic ulcer is extremely rare in that location, we went back and made numerous sections of the whole lesion. No evidence of cancer was found, and the final diagnosis was a benign peptic ulcer.

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THE GREAT ARCHITECT

His name is Time. He determines what shall survive, be improved or be developed, and what shall be destroyed, be removed or be relegated to a position of social insignificance. He calls to consult with men on all their projects, and even though he is frequently opposed by individuals, with their wealth and their legacies, his opinion eventually prevails. Man has respect for him, and reverence for the endowments that he has the power to bestow. Man watches his track and measures his passage with the utmost precision, in seconds, minutes, hours, days and years. As the years span into longer periods, arbitrary units

are marked off as standards by which men judge their own accomplishments, and with which they vouchsafe the promise of the future.

Tufts College Medical School is now completing such a unit of time; it is fifty years old. Starting as one of many, it has survived to become one of few—there were one hundred and sixty medical schools in this country in 1900, whereas there are but seventy-seven today. Its fifty years have been tumultuous ones in medical education, but from them it emerges an approved school, recognized by all state and national authorities, training one third of the students who enter approved medical schools from the states of Maine, Massachusetts, New Hampshire and Rhode Island, and already backed with a large and vigorous alumni body. Time has firmly established Tufts in the medical life of the country, especially that of New England.

Under other circumstances this fiftieth birthday would be worthy of more pretentious observation than can be accorded it this year. A simple program has been announced, which includes a short series of addresses and a few more intimate occasions, in which there will be participation by students, faculty, graduates and public representatives. A book that permanently records the first fifty years will be issued, and Time will then begin to draw his plans for the second half century.

Having been similarly and generously blessed by the largess of this great architect, the *Journal* extends to Tufts College Medical School hearty congratulations, and best wishes for the years to come.

WARTIME ACTIVITIES ARE DIFFERENT

THE Directing Board of the Procurement and Assignment Service, War Manpower Commission, in its release reprinted elsewhere in this issue of the *Journal*, calls attention to the critical shortage of nurses for wartime needs and to changes in our practices necessitated thereby. As with many other groups it is manifestly impossible to train sufficient nurses soon enough to meet the needs we are about to face. The present likelihood

that we shall be spared the bombing meted out to so many other parts of the world (yet justifiably feared by us a year ago) should not permit anyone to imagine that the national crisis has yet been reached—let alone passed.

The circumstance that so many people have so much more money than they have ever had before, with so much less to spend it on, has operated to produce an increase in demand for medical and nursing services. The only deterrents are the distinctly limited number of physicians and nurses available to supply these services, and the effect of public opinion on those tempted to indulge themselves unnecessarily in the luxuries of being ill. Both these deterrents are effective, but they can and should be made still more effective if the Nation is to muster its full potential effort. The disappearance in Great Britain of all forms of civilian psychoneurosis indicates the degree to which any population may aspire in restricting itself to bare essentials.

The statement that more changes must be planned and executed to place nursing on a wartime basis seems to be an inevitable truth. The American Red Cross has accepted the responsibility of recruiting 36,000 nurses during the coming year, and certain important duties have been assigned to the recently organized Nursing Division of the Procurement and Assignment Service. That pressure may be brought to bear by the War Manpower Commission has been amply demonstrated in other fields, and the Procurement and Assignment Service will undoubtedly reach a point at which its opinion of availability or essentiality for certain nurses will not agree with that of the nurses themselves. When this point is reached, other measures must be devised. These will be more difficult in the case of women than the various ways that have been suggested to coerce men under comparable conditions. When coercion needs to be invoked, however, the method is immaterial: the country has begun to scrape the bottom of its barrel, and there is never much of value to be found among the dregs.

All the changes being brought into field after field by this war are not going to be temporary; they may endure beyond the duration. The thought that "the service of two part-time nurses can equal that of one full-time one" has a corollary, namely, that one full-time nurse can cover the jobs of two part-time ones. It is going to be as painful to decelerate as it has been to accelerate our activities—and there will undoubtedly be some that will remain accelerated. What this war is doing, primarily, is breaking down traditions—both good and bad. The good can be restored; the bad had better remain broken. In the meantime, he who resists the changes of today must prove to the rest of the world that he is not old and decrepit.

MEDICAL EPONYM

GEE-HERTER'S DISEASE

This was described by Samuel Gee (1839-1911), physician to Saint Bartholomew's Hospital, London, in his paper "On the Coeliac Affection," which appears in *Saint Bartholomew's Hospital Reports* (24: 17-23, 1888). A portion of the article follows:

There is a kind of chronic indigestion which is met with in persons of all ages, yet is especially apt to affect children between one and five years old. Signs of the disease are yielded by the faeces, being loose, not formed, but not watery, more bulky than the food taken would seem to account for, pale in colour, as if devoid of bile, yeasty, frothy, an appearance probably due to fermentation, stinking, stench often very great, the food having undergone putrefaction rather than concoction . . .

To diarrhoea alba add emaciation and cachexia, and we have a complete picture of the disease

Twenty years later, Christian Archibald Herter (1865-1910), professor of pharmacology and therapeutics at Columbia University, wrote a book entitled *On Infantulism from Chronic Intestinal Infection* (New York, 1908). The following summary is found on page 113:

1. There is a pathological state of childhood marked by a striking retardation in growth of the skeleton, the muscles and the various organs and associated with a chronic intestinal infection characterized by the overgrowth and persistence of bacterial flora belonging normally to the nursing period. To this condition may be applied the term "intestinal infantulism."

2. The chief manifestations of intestinal infantilism are arrest in the development of the body; maintenance of good mental powers and a fair development of the brain; marked abdominal distension; a slight or moderate or considerable degree of simple anaemia; the rapid onset of physical and mental fatigue; irregularities of intestinal digestion resulting in frequent diarrhoeal seizures. . . .

R. W. B.

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DEATHS

STETSON—HALBERT G. STETSON, M.D., of Greenfield, died September 15. He was in his seventy-sixth year.

Dr. Stetson received his degree from the College of Physicians and Surgeons of Baltimore in 1895. Since 1921, he had served as medical examiner, and he was also chairman of the Greenfield school board and president of the Franklin County Public Hospital Corporation. Dr. Stetson was a former president of the Franklin County Medical Society, the New York and New England Association of Railway Surgeons, the Connecticut Valley Medical Association and the Massachusetts Medical Society. He was a fellow of the American Medical Association.

WYLIE—EUGENE C. WYLIE, M.D., of Dorchester, died September 15. He was in his seventy-second year.

Dr. Wylie received his degree from Harvard Medical School in 1895. He had been a practicing physician in Dorchester for over forty-eight years and a member of the staff of the Children's Hospital for twenty years. He was a member of the Massachusetts Medical Society and the American Medical Association.

A brother survives.

WAR ACTIVITIES

PROCUREMENT AND ASSIGNMENT SERVICE

Under the caption "Wartime Nursing Is Different," the Directing Board of the Procurement and Assignment Service, War Manpower Commission, has recently released the following statement.

It is utterly impossible to provide the necessary volume of wartime nursing service on a peacetime basis. Places where nursing is going on as usual must share with others. Nurses who have not made adjustments to wartime needs for their service should understand the necessity for their participation.

The National Nursing Council has pointed out that the value of any national plan must be judged by its usefulness at the local level, that is, where nurses live and work—in the country and in the villages, towns and cities of the Nation.

Wartime nursing is different! That inescapable fact must be generally accepted by nurses, by physicians and by hospital administrators. Energy and motion now spent in resistance to change must be released for the attack on war-created needs.

Nurses have wrought many changes, but not enough,

in the pattern of nursing service since Pearl Harbor. "We just do the best we can" is heard more frequently than "This is our plan." Generally speaking, educational programs have received more thought than service programs. Acceleration of the basic course in nursing is an outstanding example. State boards of nurse examiners have initiated others.

The principles of good nursing have not changed, but nurses are learning to concentrate on the essentials. In the analysis and administration of nursing service, radical changes are being made. Tremendously valuable assistance in caring for patients is being secured from the Red Cross nurse's aides and other volunteers as well as from paid auxiliary workers.

Thus far nursing service has not been rationed; such rationing would be complicated by the differences in individual nurses and by the degree of essentiality of needed services. Furthermore, the sharing of services is more difficult than the sharing of goods. A critical shortage of nurses exists. Over 36,000 nurses are now with the armed forces and the Red Cross has accepted responsibility for the recruitment of an equal number by June 30, 1944. Our men are receiving skilled medical care of a high order, as shown by the high percentage of recovery from injury. Skilled nursing is an important factor in such care. Then, too, the very presence of nurses near the bases of military operations has repeatedly been described as a potent force in maintaining morale.

There has been an unprecedented increase in the use of civilian hospitals. Hospitals gave 14,250,000 more days of care in 1942 than in the preceding year, and the trend still is definitely upward. This is in keeping with the rapid growth of Blue Cross (group-hospitalization) plans and the Children's Bureau hospitalization program for the care of the families of service men.

Nursing is essential to the nation's health. The national nursing inventories of nursing resources in 1941 and 1943, made by the United States Public Health Service, offer a comparison of data for the two years (Table 1).

TABLE 1. National Nursing Inventories.

CLASSIFICATION	1941	1943
Active:		
Institutional	81,708	77,704
Public health	17,766	18,900
Industrial	5,312	11,220
Private duty	46,793	44,299
Other	21,276	18,476
Inactive but available	25,252	38,746*
Inactive and not available	90,979	49,829
Totals	289,286	259,174
In Nurse Corps of Army and Navy	6,371	36,000†

*Of these, 23,576 are married and under forty.
†Precise data are not available.

The total number of nurses graduated in the intervening two years is well in excess of the number withdrawn for military service; this fact is not apparent in the inventory. The returns are apparently incomplete. Active nurses who did not return their questionnaires apparently did not realize the profound importance of the information requested. This information is the basis for present planning and safeguarding the future. The relatively small decrease in the number of institutional nurses is much less significant than the increased use of hospitals in

creating the serious shortage of nurses. The increased number of nurses in industrial nursing is, of course, not surprising.

The large number of inactive nurses who reported themselves available is encouraging. But, — they are available for what, — full time or part time? These nurses and others who are still "hidden" can make a valuable contribution to nursing resources. Although it requires a little more planning, the service of two part time nurses can equal that of one full time one. Wartime nursing puts a tremendous burden on all the administrative nurses.

The program of the recently organized Nursing Division of the Procurement and Assignment Service is as follows: to determine the availability for military service or the essentiality for civilian service of all nurses eligible for military service and to submit such determinations to the American Red Cross for use in the procurement of nurses for the armed forces, to promote plans for maximum utilization of fulltime nurses and those who are able to serve only part time, to develop and maintain a roster of all graduate registered nurses, and to develop and encourage sound methods of supplementing the work of nurses with nonprofessional personnel.

Through the War Manpower Commission, nursing will not only have the benefit of the experience in the procurement and assignment of physicians, but means will be found to interpret wartime nursing to physicians and to secure their co-operation in effecting desirable wartime adjustments.

CORRESPONDENCE

BOARD OF REGISTRATION IN MEDICINE

To the Editor: At a meeting of the Board of Registration in Medicine held on July 16, 1943, Dr. H. Quimby Gallupe, of Waltham, was re-elected secretary of the Board and Dr. Edward A. Knowlton, of Holyoke, was elected chairman.

Governor Saltonstall recently appointed Dr. George L. Schadt, of Springfield, as a member of the Board to fill the expired term of Dr. Harry L. Stevens, of New Bedford, and Dr. William F. O'Reilly, of Lynn, as a member to fill the unexpired term of Dr. Francis R. Mahony, of Lowell, deceased.

H. QUIMBY GALLUPE, M.D., Secretary
Board of Registration in Medicine

State House
Boston

ASPIRATION OF PLEURAL EFFUSIONS AND OF HEMOTHORAX WITH AIR REPLEACEMENT

To the Editor: An article in the June 12 issue of the *Journal of the American Medical Association* reflected a dependence in our armed forces on the Potain aspirator, and a device was described for aspiration by means of a piston syringe. Apparently forgotten, however, is the untested and satisfactory use of a simple siphon tube by which the fluid is made to flow from the chest to a basin on the floor by force of gravity alone.

All that is necessary is an aspirating needle attached to a rubber tube and a clamp or plug to occlude the distal end. The needle and tube are then filled with water and

the tube stopped before sterilizing. After sterilizing, the stopped end of the water filled tube is allowed to rest in a basin on the floor by the bedside, the needle is inserted in the chest, then the clamp or plug is removed and the chest fluid flows down into the basin.

This method was devised by Dr. W. W. Gannett at the Massachusetts General Hospital and was in constant use on his service during my internship in 1902. It has been employed by me, and presumably by many others, ever since in preference to the clumsy and unreliable Potain aspirator.

If one prefers, the process may be started by drawing on a piston syringe attached to the distal end of the tube. This has the advantage of yielding specimens undiluted with water. But when the tube is filled and siphonage established it is much better to allow the flow to continue steadily and gently by gravity alone rather than by intermittent manipulation of the syringe.

It is commonly recognized that in the hemothorax of through-and-through gunshot wounds it is inadvisable to apply simple aspiration with re-expansion of the wounded lung. On the other hand, there is probable advantage in removing the accumulation of defibrinated blood, provided this can be done without expanding the lung. Thus, aspiration with simultaneous creation of artificial pneumothorax is practiced. The following method, which I devised while on duty with the Harvard Unit at General Hospital No. 22, B. C. F., in 1916, was found to be practical and was used extensively at that hospital.

The principle involved is that if a closed, air-containing bottle on the floor is connected with the fluid-containing pleural cavity by two tubes and needles, and if a flow by siphonage from chest to bottle is started in one of these tubes, an automatically equal amount of air will be transferred from the bottle to the chest through the other tube. Thus the fluid in the chest will be replaced by air, but throughout the process the intrathoracic pressure will remain constant.

All that is necessary is a glass bottle of 2-quart size or larger, a two hole rubber stopper with glass tubes, fitting without air leaks, and two rubber tubes 3 to 4 feet long with an aspirating needle at one end of each, the other ends connecting with the glass tubes of the bottle. The whole assembly is sterilized together.

Some means of starting the siphonage must be provided. The simplest way is to fill one of the tubes with water and to clamp it near the bottle end before sterilizing. An alternative is to insert a three way stopcock or T tube and aspirating syringe in the course of the tube through which the outflow is to be started.

For use, the assembled and sterilized apparatus is placed at the bedside. Two points on the chest are marked and infiltrated with novocain — one rather low, and the other about two spaces higher. If any uncertainty concerning the correctness of their location exists, it is well to prove the productiveness of both by puncture with an ordinary syringe and needle. Then the needle of the tube through which outflow is to be established is inserted in the chest at the lower point, the bottle is lowered to the floor and the flow is started. If the water filled tube method has been employed, one merely releases the clamp after lowering the bottle, and siphonage by the water in the tube will insure a continuous flow from the chest to the bottle. If aspiration by syringe is applied, the tube is pinched or clamped below the T tube and fluid is drawn into the syringe, then, the tube being released, ex-

pulsion of fluid from the syringe will start the siphonage, which continues by force of gravity. The fluid of hemothorax is so thoroughly defibrinated that the flow is rarely interrupted.

Commonly, in practice, the heart is markedly displaced, so that it may be well to defer insertion of the second needle until this displacement has been somewhat reduced. Soon, however, the air replacement is started by inserting the second needle at the higher puncture-point. By listening with a stethoscope, one can hear the bubbles of entering air, which proves that the system is operating satisfactorily. In due course the physical signs of hydro-pneumothorax appear—tympany above a horizontal level of flatness. The cough of pulmonary edema, which is the usual signal for terminating simple aspirations, seldom occurs, so that usually the flow may be allowed to continue until it ceases.

Both these procedures operate by means of the negative pressure induced by a column of fluid equal in height to the distance between the chest and the floor. Variations in intrathoracic pressure, as measured by a water manometer, are surprisingly slight so that this degree of aspirating force is adequate to maintain a constant flow, since it exceeds by a wide margin any negative pressure that may occur in the chest. Moreover, the steady, gentle flow by siphonage is far less apt to cause disagreeable reactions than is the irregular, more forcible aspiration by other methods. In my opinion, aspiration by siphonage deserves general adoption, not only under primitive conditions for its simplicity but also in the best hospital practice for its other advantages.

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BOOK REVIEWS

From Witchcraft to Chemotherapy. By Sir Walter Langdon-Brown, M.D., D.Sc. (hon.), F.R.C.P. The Linacre Lecture, 1941. 12°, paper, 60 pp. Cambridge, England: Cambridge University Press, 1941. 60c.

This is a brief but thoroughly interesting story of the increasing means of healing employed in medicine from early witchcraft to the latest triumph of chemotherapy. Dr. Brown shows that the homeopathic dictum that like cures like may be traced to the sympathetic form of magic and that the forerunner of plasters and poultices was a form of contagious magic. He further points out that the old wives' tales concerning magical cures are based on witchcraft, which in turn arose from the fertility cults of organized religion. Herbal remedies were in use because chemistry had not advanced sufficiently to form any basis for rational therapeutics. Only gradually did therapeutics evolve to its present triumphant position. College libraries should find this small book a valuable addition to their shelves.

A Study of the Blood in Cancer, with Special Reference to the Needs of the Tumor Clinic. By O. Cameron Gruner, M.D. (Lond.). 4°, cloth, 100 pp., with 40 illustrations, 4 plates and 32 tables. Montreal: Renouf Publishing Company, 1942. \$4.00.

This is an odd book. It has evidently been written by a man with so passionate an interest in the diagnosis of

cancer that he will sit for long hours in the laboratory studying the many minute characteristics of blood films—fresh, stained, dark-field and so forth. Unfortunately this laudable enthusiasm has probably far outstripped the importance of these hematologic minutiae in the diagnosis and prognosis of cancer.

The author states that by studying the following features of the blood, one may arrive at a tentative diagnosis of cancer and its degree of severity: viscosity (*v*), that is, ease of spread of the blood smear; crenation of red cells (*c*); fibrin formation (*f*); granular matter (*g*); ameboid movement of the leukocytes (*a*); leukocytosis (*l*); pattern formed by the red cells (*t*); agglutinating tendency of red cells (*ag*); rouleaux formation (*ro*); auto-hemolysis (*h*); size of the red cells (*s*). The matter of intracellular granules is also discussed. These features are then qualified by degrees, and one may then arrive at a formula such as the following, which is stated to be an example of cancer:

$$v^5 c^3 f^2 g^5 a^6 l^1 t^3 (ag^4 ro^4) h^2 s^3$$

That all the above abnormalities may occur in various other conditions, that they are extremely variable and that they depend in large part on technic, cleanliness of glassware and so forth is not overemphasized.

The actual relation of these widely dissimilar features to cancer is by no means proved either statistically or clinically. To confirm or disprove the author's contentions would require years of study and careful statistical analysis. One doubts that it is worth the effort.

Infant and Child in the Culture of Today: The guidance of development in home and nursery school. By Arnold Gesell, M.D., and Francis L. Ilg, M.D. In collaboration with Janet Learned, M.A., and Louise B. Ames, Ph.D. 4°, cloth, 399 pp. New York and London: Harper and Brothers, 1943. \$4.00.

Dr. Arnold Gesell is director of the Yale Clinic of Child Development and has made notable contributions in this field since the clinic was established in 1911. Furthermore, it has become the habit of those working with children to turn to Dr. Gesell's publications constantly for authoritative information about the mental growth of infants and young children. In his latest publication the author has brought together in compact form much of the experience based on the research conducted at the clinic.

The book is divided into three parts. The first is concerned primarily with the broader aspects of the relation of growth to environmental and cultural factors. The second is a detailed description of the growing child. The third is a discussion of growth guidance, and includes much wise counsel in the training of children.

Dr. Gesell portrays throughout this book his sound philosophy concerning children and their relation to the world in which they must live. The book should be of immense value to physicians, to teachers and to anyone interested in children. One rarely finds so much sound scientific information combined with practical guidance as in this book. It can be unreservedly recommended.

Victories of Army Medicine Scientific accomplishments of the Medical Department of the United States Army By Edgar E Hume, MD, DPH, DTM and LLD 8", cloth, 250 pp, with 79 illustrations Philadelphia J B Lippincott Company, 1943 \$3.00

Colonel Hume is well known for his many contributions on the history of the Medical Department of the United States Army. This book is based on lectures given before the College of Physicians of Philadelphia and Johns Hopkins University and on the Beaumont Lecture before the Wayne County Medical Society, Detroit. The volume covers the complete record of the Medical Department and the Medical Museum of the United States Army.

Beginning in 1775, with the War for Independence and extending through World War II up to the present time, details are given in regard to the history of army medicine. Subsequent chapters deal with the *Index Catalogue* of the Army Medical Library, the Medical Museum and the School of Preventive Medicine. Colonel Hume has added, moreover, an analysis of the contributions of the Army to surgery, physiology and epidemiology and to the discovery of various diseases. Naturally, emphasis is put on the work of Walter Reed and William Beaumont, but Colonel Hume has dug out from the records numerous other contributions by various men connected with the service who perhaps are not so well known.

The book is well written, and there are numerous excellent illustrations. Title pages of important books are given as well as photographs of men grouped into certain categories, such as medical bibliographers, pioneers in photomicrography, vital statisticians, ornithologists and meteorologists. An excellent account is given of Colonel John Shaw Billings, one of the greatest of military surgeons. The appendix carries tables, giving a list of the directors of the Medical Department of the United States Army from 1775, of librarians of the Army Medical Library, of curators of the Army Medical Museum and of others. There is also a list of general hospitals, each being named for a physician who served the Medical Department. The place and time of his service and the nature of the work that he did are indicated.

In general, this is an excellent book, covering the field as it has never been covered. Although there have been histories of the Medical Department of the United States Army, particularly the one published in 1929 by Colonel Ashburn, Colonel Hume has written a different type of book—an illustrated history in a semipopular manner, based on sound facts. The book should appeal not only to the medical profession but also to the general public.

Manual of Industrial Hygiene and Medical Service in War Industries Issued under the auspices of the Committee on Industrial Medicine, Division of Medical Sciences National Research Council. Prepared by the Division of Industrial Hygiene, National Institute of Health United States Public Health Service, and edited by William M. Gafar, DSc 8", cloth, 508 pp, with 20 illustrations and 5 tables Philadelphia and London W B Saunders Company, 1943 \$3.00

This manual has been prepared by the Division of Industrial Hygiene, National Institute of Health, of the

United States Public Health Service, and presents a comprehensive discussion of industrial health problems involving organization, operation, the prevention and control of disease and the problems associated with manpower shortages. Sixteen well-qualified specialists in various fields of industrial medicine and public health have contributed to the volume, which is a desirable handbook for all engaged in caring for large groups of workers.

A Surgeon's Fight to Rebuild Men An autobiography By Fred H. Albee, MD With a foreword by Lowell Thomas 5" cloth, 349 pp, with 10 illustrations and a frontispiece New York E P Dutton and Company Incorporated, 1943 \$3.50

This is an interesting autobiography by a man who has played a distinct part in the development of orthopedic surgery in this country. He is well known for his contributions to bone graft surgery and the development of numerous mechanical devices that have made operations on bones easier and more efficient. His life, moreover, has had a certain dramatic quality particularly in his early days. For Dr Albee has not been without criticism from his colleagues, while at the same time receiving honors both from scientific bodies and from the public.

The author was born in 1876 near Wiscasset, Maine, of English and French Huguenot stock. From his grandfather Houdlette, who was an expert cabinetmaker, young Albee learned much about mechanical problems and the use of his hands in delicate work. Such problems interested him all his life, and it is not surprising that he became a highly skilled manipulator of orthopedic apparatus with a finely developed sense of surgical technique. He earned his way through Bowdoin College and later attended Harvard Medical School. While there he had intimate contacts with some of the professors and writes about Richard Cabot, J J Putnam, R H Fitz A T Cabot and M H Richardson. Under Dr Cabot's direction he worked for Dr Putnam in the old Colby Hydrotherapy Institute, taking blood pressures on patients who were being treated. Dr Richardson kept an eye on this young, green hand from the first, to use Albee's own expression, and made him prosector with John Homans, in preparation for Dr Richardson's lectures.

After leaving the Massachusetts General Hospital he began practice in Waterbury, Connecticut. While there he went to New York City every week to attend orthopedic clinics, particularly at the Hospital for the Ruptured and Crippled and the New York Postgraduate Hospital. He soon became well known even abroad and while still in Waterbury, in 1906 he fused the hip joint of a patient by a bone graft. This new method of arthrodesis brought him into the limelight and he was invited to go to Budapest in 1909, while still a very young man, to demonstrate his operation. There he was received with acclaim.

After coming home he worked hard on orthopedic surgery, particularly at the animal laboratory in Cornell Medical School where he was soon made professor of orthopedic surgery. In 1911 he first used living bone as a bone graft in the treatment of Pott's disease, basing his operation on two sound principles that have largely been widely accepted in the first place, Albee stated that the graft must be so fitted that a sound blood supply is as

sured, and secondly, that the graft must come from the same species.

The rest of Albee's life is possibly of less medical interest although more important, perhaps, to the public. He served in the Army during World War I and afterward. In addition he took an active part in the development of orthopedic surgery, not only in this country but abroad, and helped to establish international orthopedic congresses in collaboration with his foreign colleagues. In 1929, when he was president of the American Orthopaedic Association, he arranged a joint meeting with the British Orthopaedic Association in London. Subsequently Dr. Albee established a private clinic in Florida.

The book is fairly well written, but there are a number of minor typographical errors. The illustrations are in general excellent and facts of considerable historical importance are contained in this volume, particularly in the early chapters.

Brucellosis in Man and Animals. By I. Forest Huddleson, D.V.M., Ph.D. Revised edition. 8°, cloth, 379 pp., with 42 illustrations and 36 tables. New York: The Commonwealth Fund, 1943. \$3.50.

The first edition of this excellent monograph, issued in 1934, carried on the frontispiece the following prediction made by Alice C. Evans in 1918, when she discovered that *Brucella melitensis*, the causative agent of undulant fever, and Bang-Striholt's bacillus, which produced epizootic abortion in cattle, showed a hitherto unsuspected kinship: "Considering the close relationship between the two organisms, and the reported frequency of virulent strains of *Bact. abortus* in cows' milk, it would seem remarkable that we do not have a disease resembling Malta fever prevalent in this country." These words have been replaced by the equally divinatorial ones of Charles Nicolle: "Mediterranean [undulant] fever is a disease of the future."

Keeping the same title Dr. Huddleson's primitive compilation of methods for the diagnosis and study of brucellosis has grown up to a treatise giving, besides detailed technical information, a complete presentation of the historical developments and of the data gathered in recent years concerning the nature, treatment and control of the disease. The book relates that in the United States the reported cases of brucellosis in man have steadily increased from 24 in 1925 to 3427 in 1941. The prophecies quoted above are on their way to realization, since Dr. D. W. Giltner warns that brucellosis in cattle has become already three times as prevalent as was tuberculosis at the time its eradication began.

This edition ought to be read by all public-health officers, since the section dealing with sanitary problems is written by Dr. Giltner, whose qualification in this field is unmatched. Other important improvements have been introduced and recent contributions not heretofore published have been included.

The 1939 edition paved the way from the booklet issued in 1934 to the 1943 monographic presentation, which by no means contains all the information available, since many data and investigations related to immunity have not been included. In this connection, attention is called to a review on immunity that appeared in the June, 1942, issue of *Bacteriological Reviews*. A melting of both sources of information would provide a valuable body of

references. The bibliography, though yet incomplete, already embraces 500 titles. The 1943 revision is not considered by Huddleson himself as the *dernier mot* on the matter treated; however, the untiring efforts of a man who has been studying a disease for more than a quarter of a century deserve the keen interest of and a warm welcome from the research as well as the professional worker.

Synopsis of Pathology. By W. A. D. Anderson, M.D. 12°, cloth, 661 pp., with 294 illustrations and 17 color plates. St. Louis: The C. V. Mosby Company, 1942. \$6.00

This synopsis of pathology concentrates in a brief survey a tremendous number of facts. It shows that the author is able to differentiate essentials and nonessentials, and the restricted bibliographic references at the end of each chapter are well chosen. By means of frequent tables, he makes an excellent synoptic presentation, particularly in the fields of hematology and lymphatic diseases. The chapter on parasites, however, needs some amplification since no mention is made of Bilharzia and cysticercosis.

The illustrations are in general well chosen and well reproduced, but one would prefer for the demonstration of tuberculosis to students a spleen with smaller tubercles than the one which has been chosen and which so closely resembles the illustration of the spleen in Hodgkin's disease. For the purpose of ordinary demonstration of miliary tuberculosis, which is manifest with three to five magnifications, is perhaps the best.

The opinion of the reviewer approaches somewhat that of the old gambler: "Don't gamble, but if you do, take the bank." Thus, the best advice seems to be to use a standard textbook in pathology. A good synopsis, such as that of Anderson, may satisfy the student and prevent his going to the more complete sources of information.

Man in Structure and Function. By Fritz Kahn, M.D. Translated from the German and edited by George Rosen, M.D. 2 vol. 8°, cloth, Vol. 1, 341 pp., with 207 illustrations, and Vol. 2, 397 pp., with 253 illustrations. New York: Alfred A. Knopf, 1943. \$10.00 (set).

This is a popular account of the anatomy and physiology of man, illustrated by a series of remarkable pictures. Based on sound scholarship, a thorough knowledge of physiology and a style suitable for the general public, nothing of its kind has ever before been written. In the reviewer's opinion, the book is by far the best of its type. The pictures are perhaps the most remarkable part of it, and any physician in looking them over is sure to gain knowledge of some of the complex physiologic processes of the body not directly in his special field of activity.

For the public these volumes are indeed a welcome addition to the literature. The book was first published in Switzerland in 1939, and it is greatly to the credit of the publisher that he had the foresight to issue this elaborate two-volume work at the present time. A sound knowledge of the body was never more needed by the American public than now, when the problems of nutrition are in the forefront. The translation from the German is excellent, and the price of the volumes is entirely justified by the contents.

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MODERN PHARMACY AND THE MEDICAL PROFESSION*

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BOSTON

IT is unique in the meetings of your society for a representative of the pharmaceutical profession to address it. It was only a little more than a year ago—April 6, 1942, to be exact—that for the first time the American Medical Association and the American Pharmaceutical Association met in joint conference at Cleveland to discuss their mutual problems. It is, I believe, this conference that has led to the recent fuller recognition of the value of co-operation between the organizations of the two professions. Medicine and pharmacy have many common objectives, all revolving about the central theme, the preservation of the public health. Active co-operation of the professions will surely aid in accomplishing these objectives.

There is evidence that indicates the concern of each profession for the work of the other in their early days in Massachusetts. It is interesting to learn that the first pharmacist to locate in Massachusetts, Giles Firmin, was the father of the physician who delivered the first medical lectures in this locality.

Giles Firmin, Sr., came to this colony in 1633 from Sudbury, England, where he had practiced as an apothecary. His son, Giles, Jr., had come to this country in 1632 to practice medicine. The father was a valued member of the new community, serving as a selectman and as a deacon of the Boston church. His service was not long, however, as in less than a year he became ill and died.

Giles Firmin, Jr., practiced his profession in and around Ipswich, and it was he who delivered the first lectures in anatomy to students in this country. After some seven years of medical practice he decided that it was not sufficiently lucrative, so he undertook the study of theology. He wrote to John Winthrop about this decision, "I am strongly sett upon to studye divinitie, my studies

else must be lost; for physick is but a meene help." It is recorded that he completed his studies in theology and returned to England, where he was ordained and settled as a rector. It is not recorded whether he found this occupation sufficiently lucrative, but presumably he did.

A study of the history of Massachusetts in the time of the Firmins reveals that pharmacy, medicine and theology were all highly regarded professions practiced by leaders in the community. The limitations of the practice of each profession were not sharply defined, and in those early times it seems that the pharmacists practiced medicine as well as pharmacy, the physicians practiced pharmacy as well as medicine, and the ministers practiced all three. The point to be emphasized is that the professions of pharmacy and medicine were very close to each other in these early days of Massachusetts.

If one continues to peruse the local history of the two professions, one discovers that the Massachusetts Medical Society made an outstanding contribution to pharmacy when on October 3, 1805, it voted to prepare a pharmacopoeia, which was published three years later. This was undoubtedly one of the events that stimulated the work resulting in the publication of the first edition of the *United States Pharmacopoeia* in December, 1820. The present twelfth revision of this publication is a striking example of accomplishment through the co-operation of the two professions.

The greatly increased interest in drugs and medicines and in uniform standards for them that accompanied the publication of the first *United States Pharmacopoeia* resulted in another important step in the progress of pharmacy in Massachusetts—the founding of the Massachusetts College of Pharmacy in Boston in 1823, the second such institution to be established in this country. This created a substantial basis for the future progress of the profession. Dr. Ephraim Eliot was the dynamic organizer and the first president of

*Presented at the annual meeting of the Massachusetts Medical Society, Boston May 26, 1943.
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the institution, which was to become the largest college of pharmacy in the world.

In both medicine and pharmacy, education and training at that time were accomplished by the apprenticeship system. It was many years before a formal course of instruction was required for admission to their practice. This apprenticeship system, which may have been excellent in its time, became outmoded with the tremendous advances in the field of science. The professions in Massachusetts were slow in realizing this, and both medicine and pharmacy suffered from such tardiness in recognizing the obvious means by which they could continue to meet their obligations to the public. Medicine finally saw what should be done, and made the completion of a standard medical curriculum the minimum requirement for admission to its practice. Just at that point medicine in Massachusetts began to outdistance pharmacy, which until very recently has been forced to proceed without any such requirement. This has brought about the present condition in which we find that approximately half the practicing pharmacists of Massachusetts have not had the advantage of a good professional education and training in an accredited college of pharmacy. The "poor boy" or "Abraham Lincoln" argument has always been used to influence legislators to keep the requirements for admission to pharmacy as low as possible, in fact the lowest in the United States.

I cannot refrain from chiding the medical profession for its failure in past years to aid in securing sound legislation in the field of pharmacy. It was not until 1941 that a law was enacted that makes graduation from an approved college of pharmacy a prerequisite to admission to the licensing examinations. And even at that late date, at the public hearing held on the proposed legislation, a prominent member of the medical profession appeared against its enactment. The effective date of this law has not been reached, but it is to be hoped that the medical profession now recognizes the value of such legislation and will do all that it can to encourage its enforcement.

You may well ask how it is that without the benefit of favorable legislation the Massachusetts College of Pharmacy has been able to progress through the years and to become the largest college of pharmacy in the world. There are many reasons for this, but perhaps the most spectacular one is to be found in the biography of a prominent citizen of Boston.

It was during one of the final years of the Civil War that a seventeen-year-old boy whose father had been killed in the war came to Boston from the little town of Acton in search of a job. He was hired as office boy and clerk by the drug firm of Weeks and Potter. Showing remarkable ability

and industry, he earned promotions rapidly, and in some nine years he became a member of the firm. His unusual business talent and keen judgment soon led him to organize the Potter Drug and Chemical Corporation, of which he became president. Meanwhile his investments in Boston real estate had grown until he became the city's largest taxpayer. His company became an international organization, and its products under the name of Cuticura were known in all parts of the world. This man, as you have doubtless surmised, was George Robert White.

In 1916, when the Massachusetts College of Pharmacy had outgrown its quarters at the corner of St. Botolph and Garrison streets, its alumni started a campaign for funds for a new building. Mr. White was interested in this campaign and its objective and, realizing that his great fortune had originated in the pharmaceutical field, he first subscribed \$50,000 to the fund. Then, when the alumni had subscribed some \$50,000 more, he became enthusiastic over the possibilities of the project and volunteered to assume the whole cost of the building. His offer was accepted and he personally supervised the construction of the main building of the college on Longwood Avenue, which reflects his artistic taste throughout its halls of marble and bronze. This building cost Mr. White somewhat more than \$850,000.

In order that this fine structure might be permanently and properly cared for, Mr. White donated a valuable piece of downtown business property, the income from which could be expected to be ample for this purpose. Mr. White was not married, and when he died much of his fortune was left to his sister, Mrs. Bradbury. When Mrs. Bradbury died, she bequeathed \$1,000,000 to the college to aid in ensuring that her brother's gift should be maintained and operated as he wished it to be. Thus the Massachusetts College of Pharmacy became the most richly endowed college of pharmacy in the world and has been enabled to offer superior courses of instruction at a moderate cost to its students. It has made it possible for the poor boy as well as the boy of financial means to secure an excellent education and training for the practice of pharmacy.

Pharmaceutical education has made marked and substantial progress during the last twenty-five years, leaving behind it the outgrown apprenticeship and preceptorship, just as did medical education in previous years. The regular undergraduate curriculum of the colleges of pharmacy, as the result of long, careful study and development, is now one of four years and of at least thirty-two hundred hours of intensive classroom and laboratory work. The outline of the curriculum is re-

vised and published under the title, *The Pharmaceutical Syllabus*, and this is respected by educators as a work that is based on an excellent foundation. The content of the curriculum has been derived functionally from a study of the needs of the profession.

Pharmacy today is one of the most important agencies engaged in the preservation of the public health. Its responsibility is to prepare and make available all the medicines, new and old, that the medical profession may require in the scientific treatment of disease, or that may be safely employed by the public as household remedies. In order to discharge this responsibility, a tremendous modern industry has been established requiring pharmacists educated and trained to take their places in manufacturing plants, research laboratories and governmental inspection bureaus, in addition to the distribution outlets such as the thousands of drugstores, the hospitals and the public dispensaries. The modern practice of pharmacy requires a modern education and training in a college of pharmacy that has adequate facilities for its work, comparable to those of the medical school in its field. The pharmaceutical curriculum has been developed with full consideration of these responsibilities and requirements.

First, it is recognized that a good background of knowledge of chemistry is essential for those who would practice pharmacy intelligently. The curriculum provides for this with full courses in inorganic chemistry, organic chemistry, analytical chemistry, qualitative and quantitative, both gravimetric and volumetric, and finally biochemistry. These courses constitute a major subject for the student. Secondly, it is recognized that an equally good background of knowledge of biological science is necessary. This is furnished through full courses in zoology, botany, physiology and bacteriology. Thirdly, there are the courses in pharmacognosy, pharmacology and public health, in which the knowledge of chemistry and the biological sciences is applied directly to the study of drugs. Fourthly, the curriculum has a large group of courses that apply all the previously mentioned divisions of knowledge to the actual preparation of medicines. These are the courses designated under the title of pharmacy, with dispensing pharmacy as the culmination of all of them. This group of courses, as would be expected, constitutes another major subject. Finally, there are included sufficient courses in English, physics and mathematics to enable the student to carry on his studies satisfactorily.

A student who completes this curriculum has the basic education and training required to enter the practice of the profession but in addition nearly all states require at least a year of supervised prac-

tice or internship before entrance to the state licensing examinations. The student who wishes to specialize in some particular phase of the practice may continue his studies in the colleges, take graduate courses, engage in research and earn the highest of graduate degrees.

Even from this brief résumé of the principal features of the pharmaceutical curriculum, it may be readily concluded that modern pharmaceutical education is comprehensive, carefully planned and worthy of the profession for which it prepares practitioners. Further, it may be concluded that these practitioners are educated and trained to assume their share of the great responsibility of those engaged in the preservation of health.

More than ever before, the profession of pharmacy is prepared to render the following services that are of particular interest to the members of your society: to have available in every community an adequate supply of high standard drugs and medicines; to have available the knowledge, skill and equipment necessary for the extemporaneous preparation of medicines prescribed by the medical profession; to have available such a knowledge of the drugs and medicines that, through proper advice, the dangers of misuse may be averted; to have available accurate and reliable information about public health, to participate in research so that new and improved medicinal agents may be made available to the medical profession.

It is on this last division of service that I should like to comment briefly. When one thinks of research, one is inclined to think of the great foundations devoted to it or of the large manufacturers' laboratories that have come into prominence in this field. Seldom does one dwell on the possibilities of research in connection with the everyday dispensing of prescribed medicines. Yet this form of research, so helpful to the physician and his patient, is a part of the service that modern pharmacy provides, as well as the major research of the large laboratories.

In order to acquaint the members of your society with the scope of this service, the Massachusetts State Pharmaceutical Association, with the co-operation of the Massachusetts College of Pharmacy, is conducting a professional exhibit at this meeting where you may see some of the results of this work. In it you may have observed how a sticky, black tar ointment may be prepared so that it can readily be removed from the skin with warm water, when its removal is desirable. You may have seen how the ordinary sulfur lotion can be prepared so that the particle size of the sulfur is extremely small and the chemical is thus made more effective. You may have tried or tried the

odor of syrup of orange so prepared that it has the attractive, aromatic qualities of the fresh fruit. You may have noticed the solutions for the eye, prepared so that they are isotonic with lachrymal secretions and thereby more satisfactory for use. You may have seen a group of medicines made so that the diabetic patient can take them without difficulty. All these and other medicines in this exhibit are the results of pharmaceutical experimentation and research in connection with the improvement of medicines that you may frequently prescribe.

Colleges of pharmacy are offering this service and are educating and training their students so that they may provide it for the medical profession. Through refresher courses, the colleges are also endeavoring to inform practicing pharmacists of the improvements in compounding that have been discovered, so that they may make use of them.

* * *

In this brief outline of some of the features of modern pharmacy I have attempted to take

you 'behind the scenes' of the practice, showing you some of the factors that have retarded its progress and some that have aided it. I have endeavored to show you the objectives of the practice and the nature of the preparation of the practitioners who are expected to accomplish these objectives. I have told you of these things because unfortunately they are not obvious even to many within our own profession. But there are strong forces at work in the right direction, and this direction is definitely toward true co-operation in the preservation of the public health.

With more than 20 per cent of the members of both our professions in military service, the care of the civilian population is a job that can be well done only by co-operative effort; and the same is true of the planning for their care in the postwar period. Both the present war and the future peace dictate the necessity for full co-operation among the medical and related health services.

To the professions of medicine and pharmacy in Massachusetts I commend the motto *Alterum alterius auxilio eget* [Each needs the help of the other].

STUDY ON EFFECTIVENESS OF DIETARY CONSULTATION*

HERBERT T. KELLY, M.D.,† AND MYRTLE SHEPPARD, A.B.‡

PHILADELPHIA

THIS study was undertaken in 1942 among private patients in order to determine the effectiveness of dietary consultation in the correction of poor habits of diet. Eighty-five adult patients, both male and female, of varying ages, selected at random, were chosen for study.

For each of the patients, there was compiled a dietary history that included a record of food habits, dislikes, intolerances and cravings. In addition, each patient was instructed to record his weekly food intake at two different periods. The purpose in having these two questionnaires filled out was, first, to determine the value of dietary consultations and, second, to study food habits. The questionnaire contains a detailed list of types of food, with spaces for the kind and amount for each meal, as well as blanks for food and drinks taken between meals. Notes explain how the amounts are to be recorded, and additional questions cover how foods such as meat, fish, eggs and vegetables were prepared and what amounts of salad dressing were used. Each patient was

given seven such sheets, one for each day, on which to record dietary intake during one week. The first questionnaire was given to the patient at his first visit, and he was shown how to fill it out, meal by meal. When the patient returned the completed food questionnaire, it was reviewed with him, with careful attention to whether the food intake was recorded properly. The patient was then given a proper diet, adapted to his needs and based on the dietary pattern revealed in his week's record. In other words, we used as the building stones for the new diets the former good food habits and, whenever necessary, substituted good food habits for the faulty ones.

A few weeks later, the patient was given the second questionnaire, which he was requested to keep for one week, as he had done previously, recording everything consumed even if all suggestions for dietary improvement had not been followed. When this was returned, dietary suggestions were again made to the patient. It is interesting that, in the case of the second questionnaire, the patients were not nearly so co-operative as with the first. Many were reluctant to record their weekly food intake for a second time, an attitude that we interpret as a challenge

*This study was made possible by a grant from the White Laboratories, Incorporated, Newark, New Jersey.

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‡Research nutritionist, Urologic Clinic.

to improve our technic and means of approach, so that patients will appreciate an opportunity to have a second review of their diets.

In this study, inasmuch as the food consumed was not weighed but expressed in household meas-

The dietary records were computed to determine their values in protein, calories, vitamins, calcium, phosphorus, iron, acid base, fiber and water. The method used in scoring the diets was the same as reported in our previous study.¹ We did not com-

TABLE 1 *Dietary Findings, among 85 Patients, before and after Consultation*

DIETARY FINDING	BEFORE CONSULTATION		AFTER CONSULTATION		DIETARY FINDING	BEFORE CONSULTATION		AFTER CONSULTATION	
	NO OF CASES	PER CENT	NO OF CASES	PER CENT		NO OF CASES	PER CENT	NO OF CASES	PER CENT
Deficiency of protein					Deficiency of calcium				
Less than 10%	5		1		Less than 10%	1		3	
10-19%	15		5		10-19%	6		1	
20-29%	8		1		20-29%	6		4	
30-39%	4		0		30-39%	8		3	
40-49%	2		0		40-49%	8		2	
50% or more	1		0		50% or more	12		1	
	35	41	7	8		41	48	14	17
Deficiency of calories					Deficiency of phosphorus				
Less than 20%	17		16		Less than 10%	4		2	
20-29%	14		21		10-19%	7		0	
30-39%	17		16		20-29%	2		1	
40-49%	10		4		30-39%	6		0	
50% or more	8		1		40-49%	2		0	
	66	77	58	68	50% or more	1		0	
Excess of calories					Deficiency of iron				
Less than 20%	2	2	0		Less than 10%	4		3	
Deficiency of vitamin A					10-19%	8		4	
Less than 10%	4		3		20-29%	3		2	
10-19%	12		1		30-39%	3		0	
20-29%	3		1		40-49%	5		0	
30-39%	3		0		50% or more	1		0	
40-49%	2		0			29	34	8	9
50% or more	31	36	7	8	Acid base imbalance				
Deficiency of vitamin B ₁					More acid than base	4	5	2	2
Less than 10%	3		2		More base than acid	74	87	75	88
10-19%	6		7		Deficiency of water				
20-29%	15		13		Less than 20%	9		9	
30-39%	16		13		20-29%	18		14	
40-49%	16		13		30-39%	11		9	
50% or more	24		3		40-49%	12		7	
	80	94	56	66	50% or more	13		4	
Deficiency of riboflavin						63	74	43	50
Less than 10%	1		2		Excess of water				
10-19%	2		9		Less than 20%	0		0	
20-29%	8		7		20-29%	0		2	
30-39%	12		7		30-39%	1		1	
40-49%	39		8		50% or more	1	1	3	4
50% or more	69	81	41	48	Deficiency of fiber				
Weekly range of niacin					Less than 10%	15		3	
Less than 35 mg	35	40	70	23	10-19%	14		13	
35-69 mg	45	53	48	56	20-29%	20		12	
70 mg or more	6	7	17	20	30-39%	5		6	
Deficiency of ascorbic acid					40-49%	3		1	
Less than 10%	0		—		50% or more	2		5	
10-19%	1		—			59	70	40	47
20-29%	3		—		Excess of fiber				
30-39%	1		—		Less than 10%	5		0	
40-49%	0		—		10-19%	3		0	
50% or more	6		—		20-29%	4		1	
	11	13	2	2	30-39%	2		0	
					40-49%	1		0	
					50% or more	1		1	
						16	19	5	6
					Fatigue between meals*	18	21	19	22
					Unequal division of calories among meals	43	50	20	24

*Other than fruit, fruit juices and milk which do not interfere with appetite

ures, the dietary findings are not completely accurate and are approximated. However, we believe we have obtained a true picture of each patient's dietary pattern.

pute the dietary amounts of fat and carbohydrate, or of minerals and vitamins, other than those for which human requirements have been established, since the Food and Nutrition Board of the Na-

tional Research Council has not recommended optimum daily allowances for these nutrients.

We then classified the data on these 85 patients to determine how many diets were deficient, before and after consultation, in protein, calories

than did any other group, probably because they had been chronically ill and wished to correct their inefficiency in the daily pursuit of their duties.

We also considered it worth while to determine from the two series of questionnaires how many

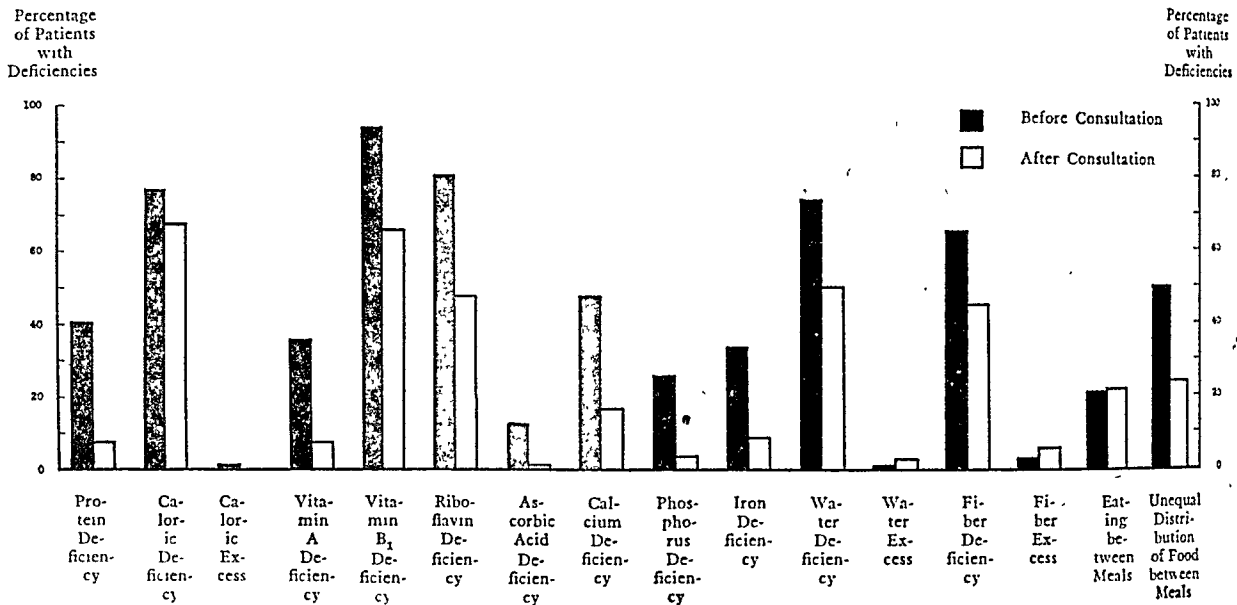


FIGURE 1. Dietary Pattern before and after Consultation.

and so forth (Table 1). In the case of niacin (nicotinic acid), we have merely given the number of diets that fell into certain numerical ranges, since data are not available for the niacin content of all foods.

RESULTS

Figure 1 illustrates the improvement in diets after consultation. In all but 8 cases the final dietary pattern was better than the original. Four of the patients whose dietary pattern was not improved by consultation were on reducing and diabetic diets and failed to adopt the dietary recommendations because of previous alcoholism and a craving for rich desserts. Another patient had a respiratory infection and could not follow the suggestions; another, who had cerebral arteriosclerosis, did not understand the therapeutic diet; still another was emotionally disturbed and had phobias regarding the consumption of rare meat (one of the "high-emotional foods"), and of vegetables unless puréed; and the remaining patient was old, with an unchangeable dietary pattern that included the consumption of too few vegetables and too much alcohol.

Interesting was the fact that the male patients co-operated more than did the female patients in submitting the second set of questionnaires. Moreover, those who were intent on gaining weight seemed to follow more of the dietary suggestions

patients daily consumed a pint of milk, one serving of meat and so forth (Table 2). In short, we were interested in knowing how many patients' diets conformed to the dietary yardstick of the

TABLE 2.

CONSUMPTION	BEFORE CONSULTATION		AFTER CONSULTATION	
	NO. OF CASES	PER-CENTAGE	NO. OF CASES	PER-CENTAGE
1 pint of milk daily	28	33	68	80
1 serving of meat, fish or poultry daily	61	72	78	91
2-3 slices of whole wheat or enriched bread (or its equivalent in cereal) daily	24	28	73	86
2-3 tbsp. of butter, cream or fortified oleomargarine daily	53	62	69	81
2 servings of vegetables daily	66	78	82	96
2 servings of fruits (one citrus) daily	57	67	80	94
3-5 eggs weekly	42	50	67	79
More than 1 cup of coffee or tea daily	50	59	20	23
Alcohol regularly	14	17	5	6
Many rich desserts	45	53	23	27

Food and Nutrition Board of the National Research Council, as well as determining several other points of general import.

The various reasons why our patients did not eat enough of the essential nutrients include allergies, ignorance of the importance of particular

foods, indigestibility of a food, constipating or laxative effect of a food, adherence to food fads, supposition that certain foods are fattening and so forth.

In this respect, the survey made by the Committee on Food Habits² regarding reasons for lack of consumption of meat is pertinent. Twenty-one per cent of 5200 subjects questioned, representing a cross section of Americans, thought meat hard to digest; 50 per cent thought some or all meat fattening.

Likes and dislikes of foods are influenced by economic background, esthetic training, traditional conflicts, national, regional, religious and age differences and differences in child-training.³ Why certain persons like one kind of food that is disliked by others is a matter that should concern the clinician and nutritionist interested in improving the nutritional status of those whom they encounter.

Even though 8 of the patients studied did not respond well to nutritional suggestions, the results may be considered good, for in 77 of 85 subjects dietary improvement followed consultation. It is significant that the patients were adults of varying ages many of whose food habits had existed for a long time, since most adult eating habits are extensions of habits formed in earlier years, usually in childhood. According to Dorcus,⁴ "Why one eats or does not eat certain foods and how these habits are modified are questions that raise problems having ramifications that lead ultimately into at least five distinct fields of psychology—physiological, social, comparative, abnormal and that concerned with the process of learning." Today the clinician, being more and more concerned with the psychology factor—since psychogenic disturbances cause so many ills—should record the patient's food dislikes and intolerances and attempt to discover whether the cause is somatic or

psychologic. In endeavoring to change food habits, one should realize that the selection of food is determined by its taste, by its ability to meet a physiologic need and by its novelty.

The results of this study show the importance of the patient's keeping a dietary record that will be reviewed by the physician. We do not consider it important that a second set of questionnaires be submitted. From time to time, it may be worth while for the physician to check the patient's diet to make certain that the changes previously suggested have been put into practice. In fact, such periodic interrogation doubtlessly acts further to encourage patients to correct faulty food habits.

SUMMARY AND CONCLUSIONS

In this study of 85 private patients the prevalence of dietary deficiencies was compared before and after dietary consultation, in order to determine the effectiveness of consultation and to study the food habits of the patients. In all but 8 cases the dietary pattern was improved after consultation. In spite of a second dietary check-up, however, there were still many dietary deficiencies, although the number had decreased considerably. Interestingly, the patients who were underweight were the most co-operative of all those studied.

Although this study was done on only 85 patients, we are convinced that dietary consultations, with check-ups from time to time, are advisable in formulating a good basic diet and in substituting good food habits for faulty ones.

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POTASSIUM SULFOCYANATE THERAPY IN ESSENTIAL HYPERTENSION*

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ANY drug whose therapeutic efficacy has been discovered, discredited and rediscovered¹⁻⁴ for forty years, and which is today widely used but is not yet included in *New and Nonofficial Remedies*, bears careful scrutiny, especially since its pharmacology is a subject of some dispute.⁴ Our experience with potassium sulfocyanate therapy covers the past thirteen years.⁵ Without reference to blood levels, the drug when first used was cautiously pushed to obtain a hypotensive action. A satisfactory fall in the blood pressure was regularly obtained in about a third of the patients under well-controlled conditions.⁵ By careful follow-up, toxic reactions were kept minimal in number, although they were at times severe in single cases. The hypotensive action was dependent on continuous exhibition of the drug. Because of the inconvenience of meticulous follow-up and the less than 50 per cent hypotensive effectiveness, potassium sulfocyanate was not regularly used until Barker⁴ and Wald⁶ pointed out the possibility of controlling the relation between toxic and therapeutic effects by following the blood cyanate level.

During the past five years we have followed 100 patients on sulfocyanate therapy for periods varying from a few months to four years. The sex distribution was 62 females and 38 males. The age range was from thirteen to sixty-eight years, 61 per cent of the patients being between thirty and fifty years of age and 20 per cent between fifty and sixty years; 12 per cent were under thirty, and 7 per cent were over sixty.

The patients were classified as Grade I (41 per cent), Grade II (37 per cent), Grade III (14 per cent) and Grade IV (8 per cent), on the following basis:

Grade I (early or mild): There is variable hypertension, the blood pressure ranging from 150 to 200 systolic and from 100 to 120 diastolic, in 23 per cent of cases falling to normal levels (140 systolic, 90 diastolic, or less) with rest or sedatives, and occasionally under stress going above the limits noted. The fundi show

minimal, if any, changes, as represented by narrowing of arterioles. The heart or kidneys show minimal, if any, changes.

Grade II (moderate): There is variable hypertension, the blood pressure ranging from 170 to 250 systolic and from 110 to 130 diastolic, usually at the lower levels, occasionally even lower, but in 11 per cent of cases falling to normal with rest or sedatives. The fundi show arteriovenous compression, narrowing, and caliber changes in the arterioles. The heart shows slight enlargement or prominence in the region of the left ventricle up to moderate enlargement, but no symptoms or signs of actual or impending failure. The urine shows no change or a slight grade of albuminuria and minimal numbers of formed elements in the sediment. The renal function is normal or slightly impaired by concentration and intravenous phenolsulfonephthalein tests.

Grade III (late benign): There is variable hypertension, with the blood pressure almost always over 170 systolic and 110 diastolic, but in 8 per cent of cases falling to normal levels. The fundi show arteriovenous compression, caliber changes in the arterioles, wide light reflexes and exudates or hemorrhages in the retinas. The heart is usually enlarged, often with symptoms of congestive or anginal failure. The urine often shows albumin and casts. The renal function is often impaired, but actual failure (uremia) is unusual. Cerebral accidents sometimes occur. This grade of hypertension is as a rule of many years' standing.

Grade IV (malignant): The blood pressure, especially the diastolic, is usually very high. The symptoms are often of recent onset in a patient almost always under fifty and often under forty, the cardinal signs being edema of the optic disks, with or without exudate and hemorrhage. Cardiac enlargement and congestive or anginal heart failure are often present. Renal impairment and failure are common.

All studies were completed at the initial and subsequent visits during the first one to three months. During this time therapeutics was confined to rest, mild sedation, — usually $\frac{1}{4}$ gr. of phenobarbital four times daily, — diet — often restricted fat and salt — and simple psychotherapy. The last cannot be stressed too much. Close interest was taken in the patient's problems and future. Rather than a brief, general reassurance, an attempt was made to instill doubt into the patient's minds about the fears for his future with which he had been as a rule preoccupied. An optimistic and hopeful attitude on the part of the physician usually engendered the same attitude in the patient. These efforts in 40 per cent of the cases resulted in a fall of 10 to 50 in the systolic pressure and 10 to 30 in the diastolic pressure.

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After this initial period of rest, sedative, diet and psychotherapy, potassium sulfocyanate (5 gr one to three times daily) was prescribed, and the blood level was checked at weekly to monthly intervals and, after an established tolerance, once in one to three months. Toxic reactions were carefully explained, the usual ones being written down for the patient's reference.

Taking the group as a whole, an excellent hypotensive action (a fall in blood pressure to below 150 systolic and below 100 diastolic) was obtained in 12 per cent of the cases. A sustained decrease of 30 to 50 systolic and 20 to 30 diastolic was obtained in an additional 16 per cent. Thus, 28 per cent of the cases showed a definite hypotensive action in addition to any fall as a result of diet, rest, sedatives and psychotherapy during the initial period. A hypotensive effect was more frequent in females (32 per cent) than in males (21 per cent). The favorable effects occurred in the different grades of hypertension as follows: Grade I 14 of 41 patients (34 per cent), Grade II 8 of 37 patients (21 per cent), Grade III 3 of 14 patients (21 per cent), and Grade IV 3 of 8 patients (38 per cent).

The most notable observation in this series was the additional symptomatic improvement from potassium sulfocyanate therapy after the usual regime of rest, diet, sedative and psychotherapy. This symptomatic improvement occurred in 53 per cent of the cases, and was greatest in Grade I hypertension. The commonest symptom and the one most effectively relieved was headache, usually hemispheric of the migraine type. Often intractable headache unaffected by other measures was brought under control. Other subjective sensations relieved were dizziness, lightheadedness and faintness, such relief being accompanied by an improvement in well being.

Approximately 20 per cent of the patients exhibited toxic effects, for the most part mild, the females showing such effects in a higher percentage (28 per cent) than the males (17 per cent). Patients were repeatedly instructed to omit the drug on the appearance of any untoward subjective sensation. As a result, the blood cyanate level was often lower than the optimum therapeutic level specified by Barker and others.^{4,7} Nevertheless toxic manifestations were kept at a minimum and were inconvenient rather than serious, and maximal symptomatic relief was commonly obtained with blood levels of less than 8 mg per 100 cc as with those above 8 mg. Of the patients not obtaining additional symptomatic relief from potassium sulfocyanate the majority received the drug in sufficient dosage to obtain a blood cyanate level of 8 to 12 mg per 100 cc and frequently higher.

The hypotensive action of the drug occurred at blood levels less than 8 mg per 100 cc in slightly over half the cases showing this reaction. Frequently the hypotensive action was as marked at lower levels as it was when the level was 12 mg or even higher. On the other hand, of the patients showing no significant response in the blood pressure, 40 per cent showed maximum blood cyanate levels of 8 mg or more and 18 per cent levels of over 12 mg.

The following is an abstract of a case showing a typical hypotensive effect.

CASE REPORT

R D (M G H U 256413) a 35-year-old man was first seen on June 24 1940 with complaints of headache, blurring of vision and edema of the ankles. The blood pressure was 190/120. The heart was enlarged with a gallop rhythm. There was dyspnea on exertion. Paroxysmal nocturnal dyspnea with red streaked sputum had been present for 3 months. The patient had had acute glomerulonephritis 9 years previously. At later visits over a period of 3 months on phenobarbital, digitalis and aspirin the blood pressure varied from 190 to 220 systolic and from 110 to 130 diastolic. On this therapy headaches continued to be almost intractable. Potassium sulfocyanate therapy (5 gr daily) was begun after 5 months on other therapeutic measures that caused no reduction in blood pressure and no relief of the headaches. At the following visit 2 weeks later there was no reduction of blood pressure but there had been no headaches. The blood cyanate level was 3.8 mg per 100 cc.

Over a period of 1 year on potassium sulfocyanate the blood pressure fell gradually from 210/140 to 140/110 (Fig 1). At no time was the blood cyanate level over 8.3 mg per 100 cc. At the end of that time however great enlargement of the thyroid gland was noted.

The patient was admitted to the hospital and studied exhaustively by the Thyroid Clinic. There was lid lag. The thyroid gland had a very hard consistency. The basal metabolic rate varied from 13 to -17 per cent. Slight exophthalmos was noted. There were a thrill and a bruit over the gland. The patient complained of excessive sleepiness. Biopsy showed an extremely hyperplastic and extremely vascular gland.

At that time potassium sulfocyanate was withdrawn. Two weeks after withdrawal the headaches were severe and the blood pressure had risen to 177/127. Aspirin failed to control the headaches. In 1 month the thyroid gland was distinctly smaller and in 2 months no nodule was palpable and the basal metabolic rate was +6 per cent.

Four months after potassium sulfocyanate was discontinued it was recommended. The headaches at once improved at a blood cyanate level of 4.2 mg per 100 cc. In 1 month the blood pressure had fallen from 172/127 to 147/99 but the thyroid gland had again begun to enlarge diffusely. In 2 weeks more it was three times normal size. The skin was normally moist but the patient was sensitive to cold. The blood pressure was 136/96.

After 2 months potassium sulfocyanate was again discontinued. Within 1 week the patient had lost his sensitivity to cold, the skin was normal, there was some exophthalmos and the thyroid gland had receded. In another

week the gland was normal in size. The patient was more alert and he was still without headache.

After another month the headaches had returned and the blood pressure was 164/108. Potassium sulfocyanate was again instituted, with prompt relief of the headaches

ing and optimistic and to utilize all resources of simple psychotherapy persuasion, suggestion, advice and direction. In this way the effect of psychotherapy has been separated from the action of

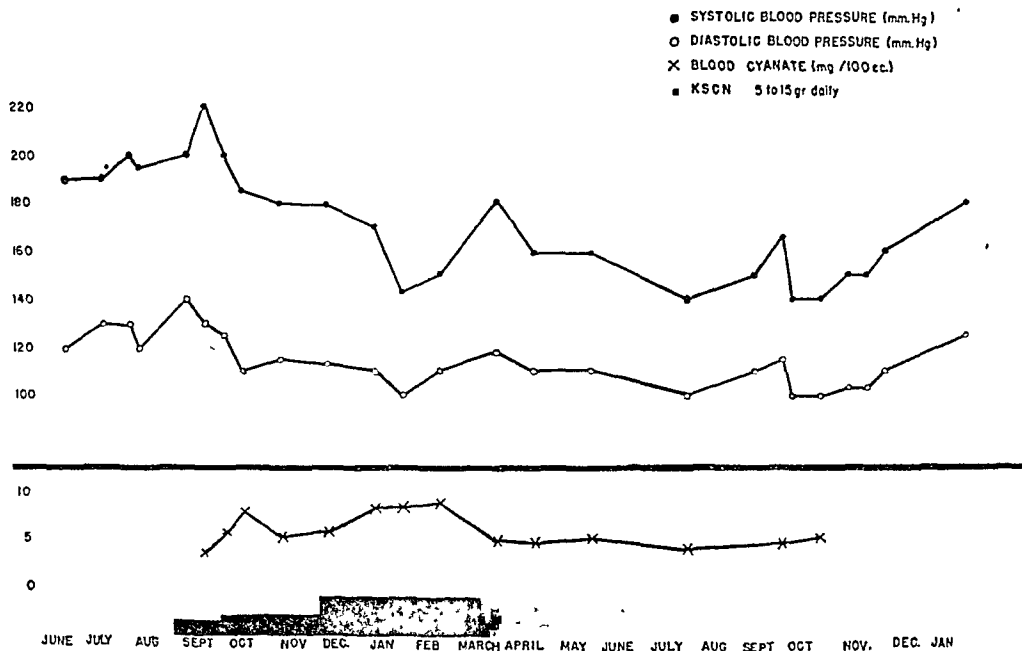


FIGURE 1.

This chart shows the systolic and diastolic blood-pressure levels, the cyanate level in the blood and the potassium sulfocyanate dosage during fourteen months of therapy.

at a blood cyanate level of 3.7 mg. per 100 cc. In 2 weeks the patient felt tired and was intolerant to cold, and lid lag was present. The blood pressure was 140/102. The thyroid gland was two to three times normal size. Again potassium sulfocyanate was stopped, the blood pressure rose, and the headaches returned.

In the past year on the advice of the Thyroid Clinic this patient has taken potassium sulfocyanate together with $1\frac{1}{2}$ to 3 gr. of thyroid daily without enlargement of the thyroid gland and with a blood pressure of 140 to 150 systolic and 90 to 108 diastolic. He has been free from headaches.

In the 3 years since the first examination the blood pressure has been controlled. The patient was given digitalis as well as potassium sulfocyanate, and there have been no notable symptoms of congestive failure, although possibly a slight loss of cardiac reserve. He has tolerated moderate work and even heavy lifting, and is continuously employed.

SUMMARY

One hundred patients with essential hypertension have been treated with potassium sulfocyanate during the past five years. This drug was given after a careful control period during which all the usual therapeutic measures were employed. Since patients with essential hypertension usually appear to be susceptible to suggestion, both favorable and unfavorable, an effort was made during the control period to be reassuring, encourag-

ing and optimistic and to utilize all resources of simple psychotherapy persuasion, suggestion, advice and direction. In this way the effect of psychotherapy has been separated from the action of the drug. The latter has been used cautiously and toxic effects have been kept to the minimum—20 per cent of the patients—but the hypotensive action has not been notable. A fall to normal or near normal occurred in only 12 per cent of the cases, and a sustained fall, although by no means to normal levels, was obtained in 16 per cent, a total of 28 per cent.

Symptomatic relief ascribable to potassium sulfocyanate alone was obtained in over half the patients, and the symptom most effectively relieved was headache, especially the very severe, intractable sort. The relief of headache is in our opinion the most valuable attribute of the drug.

Our care to avoid the toxic effects of what we consider a dangerous drug whose action is incompletely understood often prevented us from obtaining what others consider optimum therapeutic levels. Nevertheless, of the patients in this series who did not obtain additional symptomatic relief from potassium sulfocyanate, the majority attained blood cyanate levels of between 8 and 12 mg. per 100 cc. and frequently higher. Furthermore, the hypotensive action occurred in blood cyanate levels of less than 8 mg. in slightly over half of those showing this reaction. Also, of the patients showing no hypotensive action, 40 per cent

attained blood cyanate levels of 8 mg. or more, and 18 per cent levels of over 12 mg.

The case reported illustrates the better sort of result on the level of the blood pressure and on the symptoms, maintained over a three-year period during exhibition of the drug. During this time, with the additional help of digitalis, congestive failure has been controlled and at this writing the patient is gainfully employed at moderately heavy work. This case illustrates also the goitrogenic effect of potassium cyanate, the details of which are fully discussed elsewhere.⁸

Only 2 of the cases of goiter were observed in this series, both of which receded promptly after withdrawal of the drug and did not recur on readministration of the drug.

CONCLUSIONS

Potassium sulfocyanate is a potentially dangerous drug because its pharmacologic properties are

not fully understood and because the therapeutic and toxic blood levels are too close and vary too widely in different patients.

The greatest usefulness of potassium sulfocyanate therapy in essential hypertension consists in the relief of severe, migraine-like headache.

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MEDICAL PROGRESS

PHYSIOLOGY*

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PROBLEMS confronting a physician in wartime are not always new, but are often old ones acquiring new significance from the necessity of pushing personal performance far beyond the limits of normal peacetime activity, as, for example, in aviation. The attention they attract may also arise from the increased importance of certain types of disability. Thus, seasickness, which may only occasion distress in peacetime, may endanger life or may threaten the success of a military venture.

The problem of fatigue is important for both the above reasons. There is an increased and increasing demand for exertion, so that one may expect the incidence of fatigue to rise, and the costs of fatigue in terms of output and efficiency must be calculated in terms of winning or losing the war. The seriousness of the problem may also be gauged by the amounts spent by the American public on pharmaceutical products and beverages advertised as possessing antifatigue properties.

Fatigue may be defined as the progressive diminution in output resulting from the repeated performance of a given action. Such a definition is

limited, and not in accord with all pertinent data. It is limited in being conceived as a direct and proportional result of work. It fails to recognize the compensatory mechanisms that may operate to maintain output despite fatigue. Most important, however, is its failure to define the subjective aspects of fatigue, which according to some authors¹ constitute the essential feature of the condition.

The site of fatigue has been the subject of much interest, and for a number of reasons workers have been in a large measure preoccupied with the muscles.² From muscle physiology of an earlier period come two concepts that have until recently had a prepotent influence on views concerning fatigue. The first is that the various physiologic systems operate by virtue of stores of energy that are dissipated by effort and must be restored by rest. Thus, the authors of an account of chronic exhaustion in test pilots³ speak of stores of "nervous" energy that become depleted by mental strain. The second legacy from muscle physiology of a past era is the concept of fatigue products or metabolites arising from activity, which accumulate and reduce performance. There is of course no doubt that muscles are subject to fatigue, although in the presence of an adequate blood supply and at a reasonable rate of stimulation—for example, a

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maximal twitch every two or three seconds—the vigor of contractions is maintained at a relatively high level for a considerable time. With newer knowledge of the chemistry of muscular contraction, it becomes increasingly difficult to account for fatigue on the basis of accumulation of lactic acid or disappearance of muscle glycogen.⁴⁻⁶

The myoneural junction is perhaps more susceptible to fatigue than is the muscle itself, and failure of transmission at this point may account for diminution in muscular response in normal persons, as it does in victims of myasthenia gravis. The reflex centers in the spinal cord may also become subject to fatigue, especially when reflexes are elicited in too rapid succession. On the other hand, some reflexes are surprisingly little influenced by fatigue, and I have observed a single neurone discharging in the crossed-extension reflex for more than an hour without any signs of fatigue. There is considerable evidence that rhythmically discharging neurones do not become fatigued and fall out, to be replaced by other units (rotation).

When voluntary muscular effort is suspended because of fatigue, it is known that the motor apparatus is still capable of reaction, and in fact most ergograph records of a rhythmic series of muscular contractions carried to the point of fatigue show a characteristic increase in the vigor of contraction as a final effort before contractions cease.⁷ In this case the limiting factor is the central nervous system, presumably the cortex, acting under the influence of stimuli arising in the exercising muscle, which give the sensation of fatigue, exhaustion or pain. Anoxia and excessive or prolonged contraction per se are possible factors responsible for the sensory stimulation.⁸

Just what part this type of fatigue plays in the various daily occupations is not precisely known. There may be types of work in which limited groups of muscles are thus fatigued and subsequently rested many times a day; this undoubtedly occurs in persons handling tools to which they are unaccustomed. It must be less frequent in workmen who have become adapted to their tasks. On the whole, in the group of occupations calling for moderate exercise at a rate of no more than three times the basal metabolic rate, there is no evidence of this type of muscular fatigue.⁹

When the amount of muscular work is pushed to higher levels,—for example, eight or more times the basal metabolic rate,—muscular fatigue may well limit the duration of exertion. The breaking point may be determined by the muscles themselves, but frequently a limit is set by the inability of the cardiovascular-respiratory system to furnish an adequate supply of oxygen to the exercising muscles, as shown by increasing dyspnea and a

rapid rise in the pulse rate. Hypoglycemia may also determine the breaking point, through its influence on the brain rather than on the muscles, which are relatively insensitive to lack of blood sugar.

Finally there remains what is perhaps, in civilian life, the largest category, characterized by the clear absence of excessive muscular effort. Here are found the afternoon fatigue of the worker doing moderate work, the chronic fatigue of the housewife and the exhaustion of the test pilot.³ Intercurrent infections, anemias and subclinical vitamin deficiencies may well play a part in such cases, but psychologic factors most often predominate. Here, according to Bartley,¹ conflict and frustration constitute the basis of fatigue.

Treatment must be directed by an analysis of the type of fatigue in each case. Rest is the basic treatment in all types, but the duration and frequency vary. A pleasant environment, adequate diet and interesting social activities, often combined with physical activity, are essential parts of the rest period. As more is learned of the psychologic aspects of fatigue, it is being recognized that such factors as rest periods, the taking of food during working hours and a variety of other changes in working conditions operate in a substantial measure through psychologic rather than direct physiologic mechanisms. This is strikingly illustrated in a table published by Dill⁶ showing the output of a group of skilled persons working under carefully controlled conditions. It is noteworthy that practically every alteration led to an increased output; even returning to earlier conditions resulted in increases. The conclusion seems valid that optimal working conditions may be determined by factors other than purely physiologic ones, such as work and rest periods, food, lighting and heating. It can probably be assumed, however, that in the study mentioned above these factors were adequate from the start, and there is evidence that even with great motivation, output cannot be maintained if the working hours are excessively long.

A number of measures have been proposed to reduce fatigue or hasten recovery, and because of the war they are now receiving added attention. Three of these are dietary factors: carbohydrate, gelatin and vitamins.¹⁰

Hypoglycemia is not usually considered to be a factor in fatigue except as a terminal sign of exhaustion after severe and protracted exercise. When carbohydrate is available for fuel, exertion at a maximum level may be continued longer than when carbohydrate is not available, and workers have reported that ingestion of dextrose increases the ability to perform muscular work after exhaustion.¹¹ Carbohydrate feeding during rest periods has been observed to increase mechanical

efficiency in workers not subject to such extreme demands. This improvement has been attributed to psychic factors on the ground that the energy output of these workers is not sufficient to cause any significant fall in blood sugar. Hellebrandt¹⁰ concludes "that extra carbohydrate is clearly advantageous to the machine only when the work done approaches peak capacity, and that the use of sugar as a recuperative is physiologically rational only when the activity is sufficiently prolonged and vigorous to produce a hypoglycemic state." Actually, sugar is advantageous to the human machine, and is rational whenever blood sugar falls to hypoglycemic levels, whatever the type of activity or emotional state that produced the fall. The observation by Michael¹² that the blood sugar may reach low levels during a game of golf indicates that one cannot be too dogmatic about the degree of activity required to induce hypoglycemia.

Portis¹³ suggests that hypoglycemia may be a factor in the genesis of fatigue noted in neuropsychiatric patients, and believes that hyperinsulinism resulting from overactivity of the vagus nerve supply to the pancreas is responsible. He claims that there is often substantial clinical improvement on a dietary regime in which carbohydrate is not taken in the form of simple sugars and is accompanied by appropriate doses of thiamine and atropine.

An antifatigue action has recently been claimed for gelatin (60 gm. a day by mouth), but the more recent reviews on this subject indicate that evidence to this effect is not yet entirely convincing.^{11 14}

In reports of subclinical deficiencies of the vitamin B group, fatigue is one of the most pronounced symptoms, and improvement on administration of the vitamins has been noted. Just how widespread borderline vitamin deficiencies may be among workers, and how effective vitamin therapy on a wide scale would prove to be, are purely conjectural matters. Undoubtedly extensive experimentation with vitamin preparations in industrial groups is now proceeding, and definite information on this topic will some day be available. Experimental studies by Egaña et al.¹⁵ on sedentary workers taking a diet grossly deficient in thiamine indicated that deficiencies could be established within four weeks. They state that symptoms "were mild and vague, the most constant being easy fatigue, loss of ambition and loss of efficiency in daily work. There was moderate deterioration in the subjects' physical fitness for exhausting exercise, and, particularly, poor recuperation between bouts of exhausting exercise." It is hard to evaluate the subjective factors in this experiment, controls with addition of adequate amounts of vitamins to the diet unknown to the subjects and with placebo therapy not being reported. Well-controlled

studies by the same group¹⁶ on manual laborers exposed to a diet deficient in the vitamin B complex showed that the subjects began to suffer within five days a serious impairment of their fitness for sustained hard work.

Among the inorganic salts reported as of assistance in delaying the onset of fatigue are both alkalis and acidifying agents. Sodium chloride is of course invaluable in circumstances where there is salt depletion, to prevent muscular cramps. Although the success of salt therapy is most apparent in industries where work is done at high temperatures, even taking part in strenuous athletic contests may well lead to salt depletion to a harmful degree, and the danger must also be present in many military operations. Potassium salts have an antifatigue action on muscle and on neuromuscular transmission.¹⁷ They have been used in the treatment of familial periodic paralysis and myasthenia gravis, but not of fatigue.

Hellebrandt and Karpovich¹⁰ have reviewed the pharmaceutical substances advocated at one time or another to increase work or lessen fatigue. Oxygen administration prior to a strenuous but short-acting effort, such as swimming one hundred yards, seems to be helpful, mainly by increasing breath-holding ability, which permits the development of more powerful arm or leg action.

The observation that the cardiovascular system is often a limiting factor in maximum exertion has led to the use of digitalis, Coramine and Metrazol to improve maximum performance. Reports favoring the use of Metrazol are extensive.

There is general acceptance of the ability of caffeine, amphetamine (Benzedrine) and allied compounds to ward off fatigue. Apparently amphetamine is more potent than caffeine, and both operate through the central nervous system rather than directly on the muscular system.¹⁸⁻²²

The asthenia and fatigue so characteristic of Addison's disease have prompted the use of extracts of the adrenal cortex to prevent fatigue or promote recovery. Statements both claiming and denying effectiveness of cortical extracts have been made as a result of studies in normal animals and in man.¹⁰ Much better established is the influence of adrenalin or stimulation of the sympathetic nervous system to postpone fatigue or hasten recovery. Their action may be directly on the muscle, on the cardiovascular system or on the level of blood sugar.

Training is undoubtedly a key to the prevention of fatigue. Its effect is exerted both on the maximum rate of work output and on the quantity of work done.²³ The curve of maximum rate naturally tends to flatten out, and rigorous training is required to increase it thereafter. On the other

hand, the quantity of work done may increase enormously. Six to twelve weeks of daily training resulted in increases of as much as 4000 per cent in work output when the work was done at the rate of one fifth horsepower, and training increased total output 50 to 400 per cent when work was done at one half horsepower.²⁴ Other authors report comparable increases. Despite a voluminous literature, the physiology of the process remains uncertain. The muscles participate in the process, but so also does the cardiovascular system. Just what changes the heart itself undergoes remains questionable. The fact that a trained person responds to exercise with less increase in the heart rate than does an untrained person may be ascribed to changes in the heart itself or to alterations in the nervous system. Whatever the cause, this response, with the rate of deceleration of the pulse after exercise, constitutes one of the mainstays of tests of physical fitness.²⁵⁻²⁸

EFFORT SYNDROME

Discussion of fatigue and the response of the heart to exercise in trained and untrained persons naturally leads to a consideration of the so-called "effort syndrome," in which fatigue is again an outstanding complaint, and in which the heart re-

sponds to effort with an exaggerated increase in rate. If to these two signs are added breathlessness and left inframammary pain, the outstanding features of the condition have been mentioned. Wood²⁹ has listed the salient signs and symptoms of the syndrome as shown in Table 1. It has occurred to numerous observers that such a list of symptoms and signs might well be produced as the result of a widespread disturbance in the nervous system, including overaction of certain parts of both the sympathetic and the parasympathetic nervous system, muscular spasm in the muscles of the left pectoral region and alteration in respiratory movements. Secondary effects from over-ventilation are thought to account for many of the signs and symptoms, including dizziness, tendency to syncope, paresthesia, sweating and shortness of breath.^{30, 31} Although it is evident that hyper-ventilation may play a major role in producing symptoms in some persons, it may not be present at all in others; in fact, hypoventilation may occur.³²

There is a growing tendency to consider the effort syndrome as a psychoneurotic manifestation. Miller and McLean,³³ discussing the status of the emotions in palpitations and extrasystoles, say:

Palpitation is a biological manifestation of fear in the face of danger. The increased pulse rate and intensified heart action make the individual subjectively aware of the increased activity of the heart. Situations which produce palpitation involve an immediate urge to activity and at the same time a fear of it. Common examples are: palpitation experienced upon receiving a rebuke from one's superior, taking an examination, going to a forbidden amatory rendezvous and the like. In all of these situations the individual is driven by his active, ambitious attitude into an apparent danger at the same time he feels an urge to avoid. His flight is blocked.

Writing on the psychologic treatment of cases with cardiac pain, Bourne and Wittkower³⁴ take much the same position:

The data obtained confirm the view put forward previously that in cases of functional cardiac pain the pain is nearly always due to transformed anxiety arising from a conflict, unusual in intensity and abnormal in type, between menace to vital feelings and existence on the one side and self-preservation and self-assertion on the other.

It has repeatedly been remarked that the victim is often more than normally conscientious, which perhaps is of some significance from the psychologic viewpoint. The frequent and remarkable distaste for alcohol and the low incidence of venereal disease observed in victims of effort syndrome may be associated phenomena. On the other hand, it must be recognized that infection and general constitutional insufficiency are also frequent etiologic factors. Studies of the work output in the effort syndrome indicate that the reaction of patients with "true effort syndrome" is like that of convalescents from toxic-infective conditions and of constitutionally weak persons, and differs significantly from the response in those with hysteria and in the so-called "anxiety group."⁷ In a certain sense the effort syndrome may be considered to be an extreme response of "untrainedness," and the gen-

TABLE 1. Symptoms and Signs of Effort Syndrome.

SYSTEM	SYMPTOM	SIGN
General	Fatigue	Typical facies
	Nervousness	Nervous manner
Vasomotor	Palpitations	Overactive heart
	Vascular throbbing	Tachycardia
	Dizziness	Blood pressure above 150/90
	Headache	High deceleration time after exercise
	Syncope	Cold, blue hands
	Paresthesia	Visible flushes
	Flushes	Hyperpnea and tachypnea
Respiratory	Breathlessness	Frequent sighs
	Sighing	Breath-holding for less than 30 seconds
Sudomotor	Undue sweating	Palmar and axillary sweating
Muscular	Cramps	Tremor and shakiness
	Trembling and shakiness	Poor development
	Left thoracic pain	Hyperalgesia over area of pain
Gastrointestinal	Dry mouth	
	Anorexia	
	Vomiting or diarrhea	
Others	Insomnia	
	Frequency of micturition	

sponds to effort with an exaggerated increase in rate. If to these two signs are added breathlessness and left inframammary pain, the outstanding features of the condition have been mentioned. Wood²⁹ has listed the salient signs and symptoms of the syndrome as shown in Table 1. It has occurred to numerous observers that such a list of symptoms and signs might well be produced as the result of a widespread disturbance in the nervous

erally favorable response to careful training bears out this view.

PHYSIOLOGIC AND CLINICAL TESTS OF AUTONOMIC FUNCTION AND BALANCE

However satisfying it may be to be able to ascribe the majority of cases of *effort syndrome* to a noncardiac etiology, the physiologist is as yet unable to give an account of the manner in which each part of the intricate symptom-complex is developed. It is apparent that the autonomic nervous system is implicated, and that a cortical representation of that system exists through which the various peripheral effects may be mediated. Beyond this there lies a broad field for detailed study. The recent review by Darrow³⁷ entitled the "Physiological and Clinical Tests of Autonomic Function and Autonomic Balance" should prove to be a useful guide.

The problem is complicated by the following facts. In the first place, regulation in the sphere of the autonomic system occurs through the activity of two antagonistic divisions, sympathetic and parasympathetic. Although most tissues receive a double innervation, this is not universally so. Further complication is added by important exceptions to the rule that the sympathetic division is adrenergic and the parasympathetic cholinergic. Secondly, although in general there is reciprocal control of the two divisions in the central nervous system, this is not invariable, and increased activity of one division cannot be assumed to be accompanied by an equivalent reduction in the activity of the other. This is particularly so in states that impose severe strains on the organism.^{36, 37} And, thirdly, the existence of buffer or moderator mechanisms, such as the carotid sinus, adds further complications, in that these mechanisms respond to changes in autonomic activity in certain spheres by setting up vigorous reactions in an opposite direction.

These difficulties are surmounted in part by techniques that, so far as possible, isolate a single system for study. Some structures, such as the nictitating membrane of the cat, have but a single innervation. Sweat glands have only a sympathetic innervation, although their secretory fibers are cholinergic. The adrenal glands themselves are innervated by preganglionic fibers of the sympathetic nervous system, justifying the use of circulating adrenaline as an index of sympathetic activity. Other tests aim at the same effect by utilizing preparations in which one of the nerves supplying an organ is sectioned or in which the activity of one division is suppressed, as by atropine or ergotoxine. Other indices of autonomic activity employ a diametrically opposite maneuver, in which an end organ is sensitized to one or another division of the autonomic system. Drugs such as eserine or cocaine

may be employed. A particularly ingenious method is that of Beattie, Brow and Long,³⁸ who have sensitized the heart to sympathin by the administration of low concentrations of chloroform vapor. The sensitization of skeletal muscle to acetylcholine has been employed in the monkey by Bender³⁹ to reveal the liberation of that substance during emotional activity. The assay of circulating acetylcholine and adrenaline is a technic frequently employed, whereas a fruitful modification, developed particularly by Nachmansohn,⁴⁰ is the assay of acetylcholine esterase.

Darrow's suggestion that exercise-tolerance tests may be included in the category of tests of autonomic balance is worthy of consideration. In the Schneider test, for instance, low reclining and standing pulse rates are important factors in obtaining high scores. These factors, as well as the pulse-rate increment with exercise and decrement after it, are potent indications of autonomic activity, and indicate the intimate connection of physical fitness and autonomic activity.

EXPOSURE TO COLD

Warfare in cold climates and on the ocean at low temperatures has emphasized the need for physiologic studies of the influence of hypothermia, either of the body as a whole or of the extremities. Fortunately, the work of Fay⁴¹ had already contributed much to the renewed interest in the problem.

One of the most interesting phases of this development has been the reinvestigation of the response of the normal unanesthetized body to cold. The work of Cannon, Querido, Britton and Bright⁴² emphasized the dual nature of the response to cold. On exposure to cold, or when a heat deficit was produced by the ingestion of ice water, an increase in metabolism occurred, through which the deficit was made up. This increase in metabolism consisted of a moderate (13 or 14 per cent) increase in metabolism, which was regarded as due to the liberation of adrenaline, and a secondary and greater elevation induced by shivering. Objections to this evidence for a chemical factor in the augmented metabolism resulting from exposure to cold were based mainly on the difficulty of judging the moment when shivering begins.

Recent experiments, in which the onset of shivering is judged by electrical records, indicate that chemical augmentation of metabolism may not invariably be present.⁴³ The careful work of Hemingway and Hathaway⁴⁴ on trained, unanesthetized dogs places a limit of about 7 per cent on the augmentation of metabolism that occurs without shivering. An extremely interesting report is that of Odum,⁴⁵ who developed an ingenious

device to record motion in nestlings and in unhatched bird eggs. He demonstrated that homeothermic behavior does not begin until the young bird is able to shiver in response to cold. It appears that some birds are precocious in their ability to maintain the body temperature when hatched. These birds gain the ability to shiver some time before hatching. The chick appears to possess the ability to shiver at or shortly after birth, but this mechanism is not able to maintain the body temperature with efficiency until several days after hatching, presumably with the development of feathers, increased metabolism and body temperature and a more stable thermoregulator center.⁴⁶

Pinson and Adolf⁴⁷ have shown clearly that after moderate heat loss, induced by the ingestion of ice water, a nude man exposed to a room temperature of 30°C. makes up the heat deficit, solely by diminution in heat loss without increase in metabolism. On closer inspection these findings seem to accord with the experience of Cannon and his co-workers,⁴² who noted that with high environmental temperatures minimal increases in heat production occurred. Evidently heat deficits at lower environmental temperatures are required to evoke chemical augmentation of metabolism. Sex differences have also been noted: women evidently show a marked decrease in metabolism as the environmental temperature is raised, whereas men do not.⁴⁸ Apparently heat loss by sweating is less important in women than in men. The possible mechanism of the chemical regulation to be inferred from this observation has not been discussed.

In the procedure of artificial induction of hypothermia for therapeutic purposes, rectal temperatures are lowered to from 28° to 33°C. At these temperatures shivering, voluntary muscular activity and a muscular rigidity of undetermined nature are still present. Probably for this reason the metabolic rate remains above normal.⁴⁹ Blood tends toward acidity and becomes less fully saturated with oxygen. Below 30°C., possibly because of anoxia, and possibly because of reduction in blood sugar,⁵⁰ shivering begins to fail. With disappearance of shivering, production of heat diminishes and it is reasonable to assume that a further fall in body temperature will proceed with greater rapidity.

The anoxia at low body temperatures has been noted also in animals artificially cooled, and attention has been called to the possibility that many of the mental changes in hypothermia are due to anoxia.⁵¹ Walther's⁵² observation in 1862 that artificial respiration applied to rabbits cooled to 18°C. permitted their recovery even if they were left in a cool environment (10 to 12°C.) suggests that anoxia might have been responsible for the failure to

survive of animals not so treated. Randall⁴⁶ has recently observed that chicks normally cease breathing when cooled to 15°C., the heart continuing to beat at temperatures as low as 8.5°C. He states, "Administration of 100 per cent oxygen into the trachea and out by way of a punctured abdominal air sac maintained a respiratory rhythm (6 per minute) at a temperature of 10°C., indicating that hypothermic death is primarily caused by anoxic paralysis of the respiratory mechanism." There is a strong suggestion from this work that measures of revival after exposure to cold should include oxygen therapy and possibly the intravenous administration of glucose.

The renewed interest in the anesthesia and the peripheral vasoconstriction associated with hypothermia, probably first noted by Walther,⁵² has led to the introduction of local cooling, sometimes in conjunction with tourniquets, in the treatment of injuries of the extremities. Reduction of pain, prevention of bleeding, limitation of exudation, postponement of tissue necrosis by reduction of local metabolic requirements and, above all, prevention of shock are the advantages sought in this treatment. Reports^{53, 54} on the subject to date are promising, but indicate that the procedure cannot be used conveniently except on the limbs, and that cooling is not a particularly successful treatment for shock following trauma to a limb, although it appears to lengthen the survival period.⁵⁵

The cutaneous vascular responses to cold have been studied with improved technics by Hertzman and Roth.⁵⁶⁻⁵⁸ The initial response to cold is vasoconstriction. There is a reflex component, restricted to the small vessels, and found in both cooled and noncooled regions. This response is reinforced by further, delayed constriction in the same vessels in the cooled areas only, and by constriction of the large arteries in the cooled parts, apparently as a direct result of the cold. After five to sixteen minutes of vasoconstriction, a period of vasodilation supervenes. It appears after sympathectomy and after section of sensory fibers, but not after their degeneration. It has been attributed to the liberation of a histamine-like substance that excites an axon reflex. This suggestion is supported by the observation that in certain cases of excessive vasodilator response to cold, desensitization with histamine or treatment with histaminase affords a measure of relief.^{59, 60}

REGENERATION OF NERVOUS TISSUE

The ability of nerve cells to regenerate severed axons is another subject of physiologic interest receiving renewed attention as a result of the war. A recent review by Young⁶¹ provides a general account that includes most of the newer work on the subject. Evidently, the essential factor making

regeneration of function possible after severance of a peripheral nerve is the survival, in the peripheral segment of the nerve, of Schwann cells, which maintain their integrity and form small tubes down which the regenerating fibers may grow. The Schwann cells also play a leading role in bridging the gap between the cut ends of the nerve, thus providing a scaffold down which the new nerve fibers are led. Young discusses the various attempts to bridge large defects by nerve grafts to provide such tubular channels. Among the most successful of these attempts is that of De Rezende,⁶² who finds that homografts are not necessary and that formalin-fixed and stored nerves serve equally well.

The relation between rate of growth and restoration of function in regenerating nerve has been studied but little. Recently Berry, Grundfest and Hinsey⁶³ have measured the rate of conduction in regenerating fibers and have found that the fine newly regenerated fiber conducts at the slow rate of a few meters a second, and that as it grows in diameter it becomes capable of more rapid conduction. The relation between rate of conduction and fiber size discovered in adult nerves is thus found to hold for regenerating fibers.

The favorable influence of acetyl- β -methylcholine and Prostigmine on the rate of recovery of function after alcohol blocking and section of the sciatic nerve in cats⁶⁴ may indicate that the rate of growth of the regenerating fiber is increased by acetylcholine and allied compounds. It may, on the other hand, indicate a prompter recovery of function in the motor neurone supplying the cut axon. This latter supposition is strengthened by the observation of Ward and Kennard⁶⁵ that recovery of function after ablation of Areas 4 and 6 in the monkey is hastened by a similar treatment. Recovery of function in this event can hardly be expected to depend on regeneration of nerve fibers.

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NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-SECOND ANNIVERSARY

House of Delegates, May 10 and 11, 1943 (Concluded)

THE report of the Committee on Medical Education and Hospitals was then presented.

Report of the Committee on Medical Education and Hospitals

The preoccupation of all our members, with the added demands on our time and energies, and the similar conditions prevailing throughout the country have reduced the scope of this report to perfunctory dimensions.

We have no data on past postgraduate medical education or plans for the immediate future beyond the hope that if anyone can foresee the opportunity he will consider the Commonwealth Fund fellowships.

As this is written, there is still some uncertainty whether there will be fellowships available this year for physicians in New Hampshire. The amount appropriated for Commonwealth Fund fellowships this year was considerably reduced over that available in previous years, and this amount was made available with the understanding that preference would be given to applicants from the states in the South in which the Fund is carrying on its public-health program. If the number of applicants from these states is insufficient to exhaust the funds available, applicants from New Hampshire may be considered.

Because of the war situation, the number of courses available at Harvard has been somewhat reduced, but application may still be made for a month's work in obstetrics to be taken during any month in the year; for internal medicine during the month of October; and for pediatrics during the month of November or a short intensive course of two weeks' duration during August. The usual stipend of \$250 for the month's course, plus reimbursement of tuition and necessary travel expenses to and from Boston, will be offered. For the short intensive course in pediatrics, the stipend will be at the rate of \$10 a day.

It is our recommendation, however, that anyone who can anticipate finding the necessary time should make application as usual in the hope that a fellowship may become available.

JOHN P. BÖWLER, *Chairman*
JAMES W. JAMESON
HERBERT L. TAYLOR

Dr. Peters, of the Committee on Officers' Reports, moved the adoption of this report; it was so voted.

Dr. Peters then read a letter from Dr. Dolloff, of the Committee on Mental Hygiene, stating that the committee had no report to make, because of pressure of other matters and a paucity of ideas among the members of the committee. The Committee on Officers' Reports moved the acceptance of this report. The motion was carried.

The next report was that of the Committee on Public Health.

Report of the Committee on Public Health

This is the second year that the Committee on Public Health has functioned. Having started to grow up, the members are becoming conscious of the many duties that beset our particular group. War has already devastated many sections of the world, and in most living-rooms are the empty seats of sons or daughters who are already serving with our fighting forces. These facts tend to bring home the thought that we have a tremendous job ahead of us in supplying, in ever-increasing amounts, the many products necessary to carry on this titanic struggle. Of itself this obligation seems large, but add to it the needs and necessities of our allies and the proportions become so great as to be staggering; yet these are our commitments and we will carry through. This means of course a proportionate drain on man power, particularly in the industrial fields, which have constantly been depleted of their youth by the need of these men in the fighting forces. Older men and women have had to take their places in the workshops of the nation.

Loss of time means loss of ships, ammunition and other supplies vitally needed for the successful progress of the war. The industrial-health program is one of the prophylactics by which we hope to meet our responsibilities and to keep our war effort constantly on the increase.

In New Hampshire there are few companies capable of having a full-time medical department; however, many can and do have the part-time service of a doctor, with

possibly the full time services of a nurse. There are many other suggestions, such as the combined or joint services of a doctor among several different plants or units and so forth, all of which will have to be worked out in accordance with the particular set up under consideration.

The promotion of better health among our workers through education regarding sanitary and safety methods in plants, together with improvement in hygienic conditions in the workers' homes, should be part of our contribution toward victory. This can be organized along the many lines set forth by the Committee on Industrial Health of the American Medical Association, with modifications to suit our particular needs.

Your committee recommends that although our industrial efforts in New Hampshire are small as compared with those of many other states, we should keep informed on national industrial activities as they pertain to the medical man. In part this can best be accomplished by representation at the Annual Congress of Industrial Health, and the dissemination of the information gained through this meeting to our members in New Hampshire.

Using this as a basis we can spread out in our activities as our needs and circumstances permit.

HARRIS E. POWERS

Dr Metcalf then presented the report of Dr Powers as the delegate of the Society to the Fifth Congress on Industrial Health. He added that copies of the report were available to members of the Society who wished them.

Dr Peters for the Committee on Officers' Reports, recommended that the House of Delegates extend their appreciation to Dr Powers for his excellent and comprehensive report. He said that it reflects the diligence and interest applied to the papers of the meeting, and emphasized the increasing importance and value of this committee to the Society.

This motion was carried.

Dr Peters said that it was further recommended by the Committee on Officers' Reports that the House of Delegates approve continued representation at the Annual Congress of Industrial Health, and that the expenses of such delegate again be defrayed by the Society. He moved the adoption of this portion of the report.

Dr Metcalf questioned how much value the report had, adding that it had cost the Society over \$100. Dr Sycamore asked Dr Metcalf whether the cost of the report included all expenses. Secretary Metcalf replied that the total cost was \$125 including about \$25 for printing and \$100 for traveling and hotel expenses.

The motion was put to a hand vote and was lost. Speaker Parsons in answer to the question whether the enabling act could be carried out without a meeting of the House of Delegates, by sending the proposition to each delegate, stated that he could find nothing in the constitution or by-laws that covered the matter but that Chapter XV of the by-laws read

For the purpose of transacting any important business which the by-laws do not permit, the by-laws may be suspended by a unanimous vote of those present and in executive session either in the House of Delegates or in a General Session.

It would be necessary, he said, to suspend the by-laws temporarily and vote unanimously to take a vote on the proposition for the medical service corporation in that way. The by-laws did not permit the action of the House of Delegates except when in active session.

Dr Johnston moved that the by-laws be temporarily suspended for the purpose of taking a nonassembled vote on this question when the committee was prepared to present it.

Dr Parker said that the matter was of enough importance to be disposed of quickly, so that it might be possible to get a quorum at a special meeting called by the President when the time was ripe.

Dr Johnston suggested getting the consensus of the members present as to how they would react to coming to a special meeting, and some idea of how many would attend it, before entertaining any motion. The majority of those present indicated by a hand showing that they would attend. In view of this, Dr Johnston then withdrew his motion, and its second agreed.

There was no report of the Committee on Public Relations or of the Committee on Scientific Work. The next report was that of the Committee on Tuberculosis.

Report of the Committee on Tuberculosis

The phenomenal progress which has been won during the past period of twenty years in the reduction of mortality and morbidity from tuberculosis in New Hampshire and throughout the Nation is now seriously menaced. There is real danger that this fight against a devastating foe of mankind which has met with such dramatic and encouraging success may now meet with reverses.

The more hopeful workers in the campaign among whom is the chairman of your committee, are of the opinion that we cannot be certain of continued substantial reduction in mortality and morbidity within the next few years. However, it is our belief that the gains already won can be held and perhaps even further slight declines achieved. Other workers and observers have expressed the belief that the annual reductions are at an end and that definite increases are inevitable.

The reason for these forebodings is, of course, the effects of total war on the physical and mental stamina of the people with resultant lowering of resistance and consequent tendency to development of tuberculosis.

Alarming increases in the diseases are known to be occurring in all the countries at war in Europe. One of our leading public health authorities who has studied the European situation states that tuberculosis will become a plague affecting approximately 10,000,000 persons in Europe after the war.

A three point program by which the United States

could help check this anticipated plague has been outlined as follows:

- (1) Governmental and private agencies dealing with tuberculosis in this country can appraise the problem and develop the control program, for which public or private funds or both could be used.
- (2) Many American physicians and x-ray technicians who are gaining tuberculosis experience and training with the armed forces during the war could be used for postwar service abroad.
- (3) Some of the vast amount of equipment acquired by the armed forces for the chest x-raying of men entering the services could be assigned or contributed to foreign service after the war.

Wartime increases in tuberculosis are reported in England, Wales and Scotland. Particularly significant is the fact that, whereas the increases in tuberculosis deaths in adults is only 15 per cent, the increase in children approximates 45 per cent. A large part of this increase is due to tuberculosis meningitis in children. This increase indicates that English and Welsh children have been coming more and more in contact with open cases of the disease at a time when their resistance was lowered by change in diet, unaccustomed environment, poor milk, lack of sleep and frequent retreats to air-raid shelters, where the spread of tuberculosis is so easily facilitated.

In Canada the tuberculosis death rate increased in 1941.

In the United States the tuberculosis death rate in 1941 was 44.4 per 100,000 population. This figure represents a decline from the rate of 45.9 in 1940. Preliminary data for 1942 imply that the slight decline in the death rate may continue throughout our first year at war. A far different result may be the case, however, if the war should last several years and if the American people should be subjected to conditions that approximate those now prevailing in England.

During the past year a committee appointed by Governor Blood made a study of the tuberculosis situation in New Hampshire. The committee was assisted by Dr. Herman E. Hilleboe, surgeon-in-charge of Tuberculosis Control, States Relations Division, United States Public Health Service, who made a survey at the sanatoriums at Glenclyff and Pembroke, the New Hampshire State Hospital, the Laconia State School, the Mary Hitchcock Hospital, the New Hampshire Tuberculosis Association and several other organizations.

As a result, many recommendations were made for the further development of the tuberculosis-control program in New Hampshire. These include the following: an addition to the State Sanatorium at Glenclyff to take care of all patients requiring hospitalization and treatment, including chest surgery; the mass examination of all industrial workers in the State in co-operation with management and labor; the co-ordination of the activities of the several interested institutions, organizations and state departments through a representative advisory council; and the placing of the control over admittance to and continuance of hospitalization in the institutions in the hands of the State Department of Health.

The committee's report urged that tuberculosis-control efforts should be concentrated among "males 35 to 65 years of age—the persons who provide the backbone of our man power during the present emergency and the principal source of infection today."

Governor Blood in this message concurred, telling the Legislature that the greatest incidence of tuberculosis now is found in this age group, surveys in other states having

detected the disease in 1 per cent of those examined. Experience also has found that 60 per cent of those cases found were in the minimal stage, when treatment is most effective. Also pointed out was the net result that the effect of such a program would be to decrease tuberculosis in the State to the vanishing point within a few years, though showing a temporary increase at the start, which would tax the facilities available for treatment until the reduction could make itself felt.

The Industrial Hygiene Division of the State Department of Health and the New Hampshire Tuberculosis Association are now engaged in developing this program. Management and workers in a number of industries have been enlisted in several parts of the State. In the beginning, 14-by-17-inch film will be used, but plans are to secure a semiportable 35-mm. x-ray unit or a 4-by-5-inch mobile unit, which will enable the entire program to be more rapidly developed. The State Department of Health and the New Hampshire Tuberculosis Association appeal to the members of the New Hampshire Medical Society for their active support in the development of this important phase of the tuberculosis-control program.

The slogan of the sixteenth annual early-diagnosis educational campaign of the National Tuberculosis Association and its affiliated organizations is, "Follow the Example of the Armed Forces—Get a Chest X-Ray." The slogan draws attention to the fact that every man examined for the armed forces has an x-ray examination of his chest. The objective of the 1943 campaign is to emphasize that chest x-ray examination among the civilian population is just as important, and that the successful carrying out of this program can hasten the eradication of the disease.

Your committee urges more frequent use of the chest x-ray films by the physicians in New Hampshire, particularly for all patients presenting any symptoms that might suggest tuberculosis, for all who have lived or worked with a person who "took sick" with tuberculosis and for pregnant mothers. The New Hampshire Tuberculosis Association is ready to provide this service through its chest diagnostic clinics for patients referred by physicians. Also the association will provide chest x-ray films through co-operating hospitals for patients and "contacts" when the physicians so request. It should be and is the urgent desire that no person in New Hampshire needing an x-ray examination of the chest shall be deprived of the same because of lack of funds.

ROBERT B. KERR, *Chairman*
CLARENCE O. COBURN
M. DAWSON TYSON

Dr. Peters, for the Committee on Officers' Reports, moved the acceptance of this report. The motion was carried.

The next report was that of the Committee on Medical Preparedness, by Dr. D. G. Smith.

Report of the Committee on Medical Preparedness

The Committee on Medical Preparedness has continued its co-operation with the Selective Service System and has approved all appointments of physicians as examining physicians and members of the medical advisory boards.

The committee is closely affiliated with the State Committee of the Procurement and Assignment Service, which is endeavoring to secure physicians for the armed forces and at the same time retain sufficient doctors at home to take care of the civilian population. This work is becoming more and more difficult as nearly all of those under

forty five years of age and physically fit who still remain at home are either essential to the Dartmouth Medical School, are needed in their specialties or are the only physicians in their respective towns. Theoretically, replacements should be found for these men, releasing them for service in the Army and Navy, but practically there are almost no physicians suitable for replacement.

The young men have done their part in applying for commissions, but it is regretted that some of the older men have failed to realize that they must work harder than ever before to provide adequate medical service for all.

It is hoped that the House of Delegates appreciates the time and effort that the members of the county committees have given to the preparedness and procurement programs.

DEFRING G. SMITH, *Chairman*

LZRA A. JONES

CARLETON R. METCALF

The Committee on Officers Reports recommended that the Committee on Medical Preparedness remain unchanged. The motion was carried.

Dr. Peters said that the Committee on Officers Reports further recommended—and this was concurred in by two members of the committee—that the House of Delegates express their appreciation to Dr. D. G. Smith for his devotion to his duties on the Committee on Medical Preparedness, multiple as they were, and undoubtedly at a personal sacrifice in the performance of this work. He moved the adoption of this portion of the report. The motion was carried.

It was voted that the reading of the Necrology Report be dispensed with, since it would appear in the Transactions.

The next business was the selection of the place of the next meeting. Dr. Dye moved that the Society express its gratitude to the Manchester group and that the next year's meeting be held at Manchester. The motion was carried.

Dr. Berudoin moved that Dr. T. C. Pulsifer be made an affiliate member. The motion was carried.

The next report was that of the Committee on Maternity and Infancy, by Dr. B. P. Burpee.

Report of the Committee on Maternity and Infancy

This year marks the ninth in the study of maternal and infant deaths in New Hampshire by the Committee on Maternity and Infancy. This year again the maternal death rate is lower than that of 1941, as are the infant death and stillbirth rates. The committee has endeavored, as in the past, to study and analyze all available data on the maternal deaths of 1942, and to appraise these data so far as possible, having the advantage of knowing the result of a procedure and not having to decide the actual course to be taken. The committee realizes that it is much easier to decide what should have been done in a certain case retrospectively than it is to be confronted with the actual problem and have to decide what course to pursue. It is with this thought in mind that we wish physicians to read these recommendations and suggestions made. It is the committee's thought that such comments

as are made may be of value to all physicians who may at any time have similar cases. It is realized too that there are situations where two avenues of approach are present, or seemingly present, and it is up to the attending physician to choose the one that seems to him the best, if the approach used by him fails, he can only wager that the other approach would have given a better result.

The information for this study was gathered from physicians and hospital records. It has been a little more difficult in obtaining the necessary data this year, owing to the fact that some of these physicians are in military service and their hospital records, in some cases, are incomplete. In 1 case only were there insufficient data for the committee to classify it in one of three groups.

It is gratifying to all to see a reduction in the maternal death rate, the highest over a period of ten years being 13.3 per 1000 live births in 1933.

The greater portion of deaths were classified as unavoidable, which is encouraging, but we must point out that 3 of these had been treated by out of state physicians and had been sent over the border in such a physical condition that these deaths were unavoidable to the extent that the New Hampshire physician was involved. In all 3 cases, from information gathered as to care given by the out of state physician, it would seem that the care was inadequate. This situation may work in reverse—that is, patients go into other states for final treatment, having received inadequate care in New Hampshire, so perhaps we are not justified in trying to make our maternal death rate appear lower.

As yet, not much has been done in the study of infant deaths in this state, mostly for the reason that it would be too much of a task for this committee to gather data complete enough on each case to make feasible recommendations. The deaths have merely been tabulated according to causes, these causes having been taken from the death certificates.

Stillbirths have also been tabulated according to causes. The definition of a stillborn child now in general use in the United States, and the one accepted by the Children's Bureau, the American Public Health Association and the Bureau of the Census, has been adopted by New Hampshire and will be found in the section on stillbirths. The problem of stillbirths is a real one, not only for New Hampshire, whose stillbirth rate compares favorably with many other states, but for the United States as a whole. Even though the Bureau of the Census issues statistics, the whole story cannot be told by figures, as there is no single definition of a stillbirth in universal use. The period of gestation, which must be reached before registration as a stillbirth is required, differs in each state.

MATERNAL DEATHS

There were 15 maternal deaths in 1942, which is 2 less than in 1941, and the lowest number recorded since this study began. In 1942 there were 9599 live births thereby giving a maternal mortality of 1.6 per 1000 live births. It is to be noted that there were 914 more live births in 1942 than in 1941. This was expected, owing to the influx of people into New Hampshire to the defense area, and to the increased number of marriages on the part of those men leaving for military service.

These 15 maternal deaths have been classified according to the *International List of Causes of Death* (fifth revision). This classification was made on the basis of what the attending physician placed on the death certificate as the cause of death.

CLASSIFICATION No.	No. OF DEATHS
147 (b) Puerperal sepsis	3
148 (b) Puerperal nephritis	1
149 (b) Difficult delivery with hemorrhage	1
147 (c) Puerperal thrombophlebitis	2
140 (b) Abortion with infection	1
141 (a) Abortion without infection — hemorrhage	1
144 (b) Toxemia — nephritic (death before delivery)	2
142 (a) Ectopic gestation	1
150 (c) Other and unspecified conditions of childbirth — asphyxiation due to inhalation of foreign matter	1
146 (c) Postpartum hemorrhage	2
Total	15

The committee has reclassified these deaths for the purpose of this report on the basis of data presented in the following way:

CAUSE OF DEATH	No. OF DEATHS
Accidents of pregnancy	5
Puerperal embolism	2
Ectopic gestation ruptured	1
Asphyxiation — inhalation	1
Acute pulmonary edema	1
Post-partum hemorrhage	4
Following spontaneous abortion	1
Retained placenta	1
Cause undetermined	2
Toxemias (all types)	3
Puerperal sepsis	2
Abortion (self-induced with resulting bacterial endocarditis)	1
Total	15

There were two cesarean sections done in the 1942 series. One was considered as justifiable and the data on the other were insufficient for the committee to make any comments. Of these 15 deaths, 4 autopsies were obtained, 3 of which confirmed the diagnosis made by the clinician. In 1 autopsy the cause of death could not be determined, but a complete autopsy was not done since permission to examine the head was not given. The committee from the data obtained classified this as an accident of pregnancy, probably acute pulmonary edema.

It has been the usual procedure of this committee to classify these deaths further, just by way of making the problem more concrete and to try to point out to what extent clinicians can be held responsible in helping to lower maternal deaths. Group I includes the cases in which the patient was at fault because of refusal for prenatal care, neglect, self-induced abortion and so forth; Group II, those in which the obstetric treatment was inadequate; Group III, those which were apparently unavoidable; and Group IV, those where data were insufficient and, therefore, undetermined.

CLASSIFICATION	No. OF DEATHS
Group I	3
Group II	4
Group III	7
Group IV	1
Total	15

The causes of death in Group I, where the patient was at fault, were as follows:

CAUSE OF DEATH	No. OF CASES
Toxemia of pregnancy (neglect of treatment)	2
Induced abortion	1
Total	3

The causes of death in Group II, where it was considered that inadequate care was given, were as follows:

CAUSE OF DEATH	No. OF CASES
Post-partum hemorrhage	2
Puerperal thrombophlebitis with pulmonary embolism	1
Difficult delivery with puerperal sepsis	1
Total	4

The causes of death in Group III, in which the death were considered unavoidable, were as follows:

Asphyxiation due to inhalation	1
Phlebitis with embolism	1
Post-partum hemorrhage	2
Ruptured ectopic gestation	1
Puerperal sepsis	1
Toxemia	1
Total	7

The toxemia listed in this group was one of those that had been treated out of state and was first seen by a New Hampshire doctor when the patient was having sustained convulsions and died within a few minutes. An immediate cesarean was performed and a live baby delivered. The case of puerperal sepsis was one of those seen by a New Hampshire doctor in the terminal stage. In both these cases, the committee considered them unavoidable since this particular study is to comment on the grade of obstetrics being done in the State, as is evidenced by the analysis of these particular cases.

Only one case must be put in Group IV because of insufficient data. The cause of death given was puerperal sepsis following cesarean section.

In the numerical analysis, the group of unavoidable deaths is the greatest, and the order of causes of death are accidents of pregnancy, post-partum hemorrhage, toxemia, puerperal sepsis and induced abortion with resulting endocarditis.

In the 1942 series all cases were delivered in a hospital. The deaths by county in urban and rural areas were as follows:

COUNTY	URBAN CASES	RURAL CASES	TOTAL
Belknap	1	0	1
Carroll	0	0	0
Cheshire	0	0	0
Coos	0	2	2
Grafton	3	1	4
Hillsborough	2	0	2
Merrimack	0	0	0
Rockingham	3	1	4
Strafford	0	0	0
Sullivan	0	2	2
Totals	9	6	15

The maternal mortality rates per 1000 live births by years from 1933 to 1942, inclusive, are as follows:

YEAR	No. OF DEATHS	RATE PER 1000 LIVE BIRTHS
1933	6	6.3
1934	5	5.4
1935	46	6.1
1936	37	4.8
1937	34	4.3
1938	24	3.8
1939	25	3.1
1940	24	3.1*
1941	17	1.9*
1942	15	1.6

*Corrected rates.

The most recent figures available for maternal death rates are those of 1940. At that time the maternal death rate for the United States as a whole was 3.8 per 1000 live births. North Dakota had the lowest maternal death

rate, 17, and South Carolina the highest, 68. New Hampshire for 1940 was in nineteenth place with a rate of 31. We have no comparable figures for 1941 and 1942.

Comments and Recommendations

The committee, having reviewed all the available data reports that in no case was there evidence of really bad obstetrics. In most cases, it was a matter of not giving enough treatment, rather than the wrong kind. This appeared to be true in the 2 cases of post partum hemorrhage, and at this time the committee would like to make certain comments on the treatment of such cases.

The committee would like to emphasize once again the necessity of proper diagnosis and immediate treatment of those women who suffer hemorrhage or who show signs of shock immediately or soon after delivery, whether the delivery has been spontaneous or operative. One must remember that uterine atony is not the only cause of post partum hemorrhage, and more especially of shock without evidence of external bleeding.

Other pathologic conditions may be a partially separated placenta, retained cotyledons of a removed placenta, cervical tear, tear of the lower segment or body of the uterus and, less frequently, inverted uterus, fibromas and ruptured vaginal varicosity. These may all cause profuse bleeding.

The conditions that may cause profound shock without external bleeding are tear of the lower uterine segment, rupture of the uterine body and inverted uterus.

Each of these conditions is serious enough to justify immediate sterile vaginal examination, both manual and visual, to establish correct diagnosis, the specific treatment to follow depending on that diagnosis. Partially separated placenta and retained cotyledons should be removed manually. Cervical lacerations should be repaired under direct vision. A ruptured uterus requires abdominal surgery, either to repair the rent, if possible or to do a hysterectomy. Fibromas with persistent bleeding may also necessitate hysterectomy. An inverted uterus requires replacement either manually from below or by abdominal surgery. Ruptured vaginal varicosities may be controlled by packing tightly. In addition to these briefly outlined specific treatments, the committee would like to reiterate the immense value of intravenous fluids, especially transfusions of whole blood or plasma.

It is thought worth while to stress the importance of keeping confined to bed a patient who shows clinical evidence of a phlebitis, particularly in the presence of a septic temperature, regardless of how low grade until the temperature becomes normal and remains normal and the signs and symptoms clear. There is a great tendency on the part of physicians to disregard these warnings and to get these patients out of bed, only to have them die in a few minutes.

One death was due to inhalation of vomitus while being delivered. Although this was considered unavoidable it does nevertheless remind us that we can be more careful in explaining to patients the importance of not eating heavily, or not at all, if there are signs and symptoms of going into labor.

The 2 cases of death due to toxemia were classed in Group I that is the patient being at fault. In both cases, the patients were being seen regularly and being given good prenatal care. Both patients were more or less toxic throughout, and both neglected to report back to the physician when told to do so. Both were severely toxic

when finally seen. The committee wishes to point out that the fault does actually lie with the patient, but can a physician who is giving good prenatal care forget about a toxic patient? In most cases, it would be easy to contact this patient either by telephone or letter or by sending out the district nurse or public health nurse and asking her to check on these patients or to see that they come in to their doctor. These nurses are placed in the field to help physicians as well as patients. It is up to the physician to educate his toxic patient as to the value of frequent prenatal visits.

The committee must continue to comment on the value of hospital records and the necessity of keeping these up to date. For the most part, hospital records, when resorted to for information this year, were most in complete. To be sure most of these incomplete records were those of physicians who had gone into the armed services and were undoubtedly too busy at the last to think of hospital records. There are also incomplete records of physicians who are not in service. The one case classed in Group IV is an example of the latter. From the hospital record it can be gathered that the infant was delivered by cesarean section and that the mother died two days post partum. No reasons for performing a section were given. It seems necessary to keep stressing the subject of records. Keeping poor records helps to lower the standard of the hospital. It is as much the hospitals' responsibility to see that their records are kept up to date as it is the physicians'. Good records are a safeguard for both physicians and hospitals.

MATERNITY CARE PROGRAM FOR SERVICEMEN'S WIVES

The committee served this year, as before, as an advisory committee to the State Board of Health regarding programs involving the care of mothers and infants. The purpose of this procedure has been to afford proper representation of the Society regarding such programs.

With the induction of thousands of young men from New Hampshire into the armed forces it became apparent that provisions had to be made for the care of pregnant wives of these men. The committee was confronted with the problem of aiding the State Board of Health in meeting this emergency. The following facts are presented for the information of the Society.

The First Deficiency Appropriation Act of Congress in 1943 provided for a sum of money to be allotted to any state setting up a program for maternity care of wives of servicemen. New Hampshire has such a program now in operation, administered by the State Board of Health through the Division of Maternal and Child Health. As to eligibility for care under this plan, Any woman in the State irrespective of legal residence, whose husband is an enlisted man [this includes men deceased or missing in action] in the armed forces of the United States of the fourth, fifth, sixth and seventh grades [Army, Navy, Marine Corps and Coast Guard], and who makes application for such care will be eligible for the medical and hospital maternity services provided under the plan, without cost to the family, when similar services are not otherwise available from the medical or hospital facilities of the Army or Navy or from facilities provided by or through official state or local health agencies.

Application forms for this service have been distributed to physicians, hospitals, the Red Cross and other social agencies throughout the State and more may be obtained from the State Board of Health.

The service gives prenatal, delivery and post-partum care, and hospitalization on ward service at a flat rate at present of \$45 for a ten-day period. Physicians are paid on the basis of \$15 for prenatal care and \$20 for delivery. This fee was recommended by the Committee on Maternity and Infancy of the Society.

Applications must be returned to the Division of Maternal and Child Health, 17 School Street, Concord, and on receiving the application, authorization for this care will be sent to the physician and hospital involved. The plan is not retroactive; all care must be authorized before financial responsibility for the case can be assumed by the Division of Maternal and Child Health. In case of an emergency delivery, this department must be notified within forty-eight hours.

Hospitals to be used under the plan are those which are duly licensed by the State Board of Health to admit and care for maternity patients. Home deliveries are to be done at the discretion of the attending physicians. Only those physicians who are graduates of a recognized medical school, have an M.D. degree and are licensed to practice medicine in New Hampshire may be authorized to give medical care under this plan.

Any further information regarding this plan may be obtained from the State Board of Health.

INFANT MORTALITY

Included in this group are those infants who died under one year of age. There were 322 infant deaths in 1942, giving an infant death rate of 33.5 per 1000 live births. In 1941 there were 319 deaths, a rate of 33 per 1000 live births. These deaths are tabulated as to causes and time of death after birth.

CAUSE OF DEATH	No. OF DEATHS
Deaths occurring during the first day:	
Prematurity	87
Congenital deformity	29
Atelectasis	12
Intracranial hemorrhage	7
Birth injury	4
Toxemia	2
Prolapse of cord	1
Hemorrhagic disease of newborn	1
Total	143
Deaths occurring during the first month exclusive of the first day:	
Prematurity	20
Congenital deformity	16
Pneumonia	7
Atelectasis	5
Asphyxia	2
Hemorrhagic disease of newborn	7
Intracranial hemorrhage	5
Enteritis	2
Septicemia	1
Hydrothorax and edema	1
Meningitis	1
Syphilis	1
Unknown	1
Total	69
Deaths occurring from the second to the twelfth month, inclusive:	
Pneumonia	33
Malnutrition	10
Congenital anomaly	10
Gastroenteritis	9
Suffocation (accidental)	8
Influenza	2
Intussusception	2
Pyelonephritis	1
Septicemia	1
Tubercular meningitis	2
Pyloric stenosis	2
Osteomyelitis	1
Unknown	4
Total	85
Unclassified owing to late reporting	25

There has been a steady decline in infant mortality in the United States as a whole since 1915, when data on this subject were first collected. The rate then for the country as a whole was 100 per 1000 live births, and in 1938 it was just half, 50 per 1000 live births. The better control of communicable diseases and a better understanding of infant feeding, thereby decreasing gastrointestinal disturbances, have probably contributed greatly to this decrease. It is interesting to note, that, so far as figures can be obtained, New Zealand has consistently reported a lower infant death rate than any other country, whereas the Netherlands, Australia, Norway, Sweden and Switzerland have reported rates that have been lower than those of the United States, according to the last obtainable figures (1936).

For the year 1936, in the United States the causes of deaths of infants under one year of age, as compiled from the death certificates, showed that 52 per cent died of prenatal and natal conditions. These conditions included prematurity, injury at birth, malformation and debility. From 1915 to 1936, where figures are available, deaths under one year have been cut in half, deaths during the first month have been reduced one fourth, and deaths occurring on the first day have shown no decrease.

Our own series of infant deaths bear out some of these facts, namely, that the death rate for those during the first day of life remains high. In the United States as a whole the rate in 1915 and 1936 was 15 per 1000 live births, and New Hampshire also shows 15 per 1000 live births in 1942. The New Hampshire series also shows that over 50 per cent are attributable to prenatal and natal conditions. Adair and Potter point out in their book *Fetal and Neonatal Death* that the classification used by the Bureau of Census, which is an international one, classifies all conditions under one of five headings, namely, congenital malformation, congenital debility, premature birth, injury at birth and other diseases peculiar to early infancy. Congenital debility usually indicates that the physician was uncertain as to the cause of death. Prematurity usually takes precedence over contributing causes of death on a certificate, thereby possibly masking the real cause of death. On the basis of this classification, they believe that the figures from the Department of Vital Statistics are inaccurate for actual frequency of the various causes of death in early infancy.

The infant mortality rates per 1000 live births by years are as follows:

YEAR	RATE
1935	54
1936	47
1937	48
1938	48
1939	45
1940	32
1941	33
1942	33.5

STILLBIRTHS

Of the 244 stillbirths recorded in the State for 1942, the following causes were given:

CAUSE	No. OF CASES
Unknown	67
Prematurity	44
Toxemia	36
Hemorrhage, maternal	31
Congenital deformity	30
Attributed to cord	19
Difficult delivery	8
Syphilis	3

Hemorrhage fetal	2
Atelactas	1
Therapeutic abortion	1
Erythroblastosis	1
Diabetes	1
Total	244

Stillbirths vary from year to year, and no evidence for this variation is apparent. For the last five years the figures are as follows:

YEAR	NO OF CASES
1933	242
1939	211
1940	187
1941	201
1942	244

Previously, New Hampshire has used the definition of a stillbirth recommended by the League of Nations and the International Institute of Statistics—namely, 'A dead birth (stillbirth) is the birth of a (viable) foetus, after at least twenty-eight weeks pregnancy in which pulmonary respiration does not occur, such a foetus may die either (a) before, (b) during or (c) after birth, but before it has breathed.' The statistical definition adopted for use in the United States, and the one accepted by the Children's Bureau, the American Public Health Association and the Bureau of the Census and the one now in use in New Hampshire, is as follows: 'A fetus showing no evidence of life after complete birth (no action of heart, breathing or movement of voluntary muscle), if the twentieth week of gestation has been reached, should be registered as a stillbirth.'

The differences between these two definitions relate to the period of gestation required and to the criterion for determining life. Since the point of differentiation between liveborn and stillborn is highly controversial, the final decision as to the definition of stillbirth really rests with the obstetrician who is to make the decision in actual practice. If these physicians would voice their opinion on the controversial points involved, it would aid the State Board of Health and Vital Statistics Office in becoming aware of the desires of the medical profession in regard to this subject. Meanwhile in order to make uniformity in reporting for the purposes of comparison, it seems essential that physicians follow the United States definition.

As has been said, there is no single definition of still birth in use in the states, the period of gestation differing widely in different states. In Maryland, Missouri and New York City the delivery of any product of conception must be registered, in Delaware there is no definite ruling, in Connecticut registration is not necessary unless the period of gestation is seven months or more. In the majority of states, a fetus that has advanced to the fifth month must be registered.

It is, therefore, evident that there is a lack of comparable bases for analysis. The stillbirth rate for New Hampshire for 1942 is 25.4 per 1000 live births. We have no available figures for the United States except for 1939, which showed 32 stillbirths per 1000 live births. The highest rate was in Mississippi, 51.1, and the lowest was in Washington, 17.5.

In 1936, the Children's Bureau conducted a study of the maternal and fetal conditions associated with stillbirths for the purposes of determining and classifying the causes of death. The study was made on 6750 stillbirths, and certain interesting figures were obtained. It showed, among other things, that 58 per cent of

the fetuses die before the onset of labor and 42 per cent during labor, that in the early months of pregnancy deaths before the onset of labor were proportionately higher than deaths during labor, that the greater per cent of fetuses died before labor began in those cases where toxemia, hemorrhage and syphilis were maternal complications, and where deformities were found in the fetus. In this series it was found that the following conditions were associated with stillbirths in the order of frequency: toxemia, ante partum and intra partum hemorrhage, cord complication or anomaly, congenital malformation, syphilis and birth injury.

For the most part the causes of fetal death as given on death certificates are maternal conditions with the exception of fetal deformities. Here again the classification of causes of stillbirths varies. The International Commission for Revision of the International List of Causes of Death in 1938 adopted the following classification: Group I, stillbirth caused by disease in, or accident to, the mother; Group II, anomalies of the fetus, placenta or cord; Group III, death of the fetus by injury or other causes, and Group IV, stillbirth due to other causes.

The purpose of the committee in going somewhat into detail on stillbirths is to try to stimulate the interest of physicians in this problem. Any comments as to the definition of a stillbirth or as to the causes of stillbirth will be gratefully received by the committee.

The committee wishes to thank the physicians and hospitals for their continued co-operation in furnishing the data necessary for making this report. Any recommendations that the physicians throughout the State may have to make regarding these annual reports will be greatly appreciated.

The committee wishes to acknowledge with appreciation the co-operation of the Division of Maternal and Child Health of the State Board of Health in furnishing data and personnel in the preparation of this report.

ROBERT O. BLOOD, Chairman
BENJAMIN P. BURPEE
MARION FAIRFIELD

Dr Burpee then read a letter from Dr Mildred A. Chamberlin, acting director of the State Board of Health, which requested an interpretation of a paragraph in the regulations governing the maternity care program for servicemen's wives. This paragraph read as follows:

Authorization for medical or hospital care is to be made by the State Board of Health under agreement with the attending physician or the hospital that no payments will be accepted from the patient or family.

The Board of Health believed that the patient should be allowed to contribute, if she so desired, and asked if this was prohibited by the rule in question. After a lengthy discussion, Dr Peters reported that the Committee on Officers' Reports thought that they did not have enough information to bring in any definite recommendation regarding this matter, other than to recommend that the House of Delegates consider the Government plan for the payment of hospital and medical care of servicemen's wives at the time of deliv-

ery. He moved the adoption of that portion of the report; this motion was carried.

Dr. Burpee said that the State Board of Health would also like advice on the matter of stillbirths. There was still a great deal of argument going on as to what should constitute the definition of a stillbirth. Previously, New Hampshire had used the definition recommended by the League of Nations and the International Institute of Statistics: "A dead birth or stillbirth is a birth of a fetus after at least twenty-eight weeks of pregnancy, in which pulmonary respiration does not occur. Such fetus may die either before, during or after birth, before it has breathed." The statistical definition adopted in the United States and the one accepted by the Children's Bureau, the American Public Health Association and the Bureau of the Census, and the one now in use in New Hampshire, was as follows: "A fetus showing no evidence of life after complete birth, no action of heart, breathing or movement of the voluntary muscles, if the twentieth week of gestation has been reached, it should be registered as a stillbirth." He said that the State Board of Health would like an expression of opinion from the doctors of the State as to what definition of a stillbirth should be used.

Dr. Wilkins asked whether the definition now being used was not satisfactory. Dr. Burpee replied that it was satisfactory to some people but not to others. Any fetus, he said, that was born after the twentieth week was considered a stillbirth. Speaker Parsons asked Dr. Peters whether he had a report on this matter.

Dr. Peters moved that the Committee on Maternity and Infancy take the matter up with the Public Health Department for further clarification. This motion was carried.

Dr. Peters for the Committee on Officers' Reports, further moved that the report of the Committee on Maternity and Infancy be accepted. The motion was carried.

Speaker Parsons said that Dr. Burpee had asked for an opinion from the delegates on the question of medical fees in obstetric work, assisted by government grant, and asked whether there was any further discussion on the matter.

Dr. McGregor said he thought the fee was too low.

Another member asked whether the \$15 and the \$20 fees were standard ones. Dr. Smith said that the chief objection of the Nashua doctors was that the State Board of Health, the Government and the Children's Bureau were dictating fees, and they did not see why they could not charge more and have the patient pay the difference between the charge that they might make and what the Government would give under this appropriation. If that didn't occur, they would

rather not accept any money from the Government or the State Department of Health and take their chances of collecting the regular fee from the patient's family or the patient. For that reason, they were crossing out that agreement at the bottom of the application.

Dr. Smith said further that his authority for the investigation of these cases by the Red Cross was given by the field secretary of the Red Cross in New Hampshire, and also that Dr. Chamberlin in a letter in February asked that the Red Cross investigate. One of the doctors also stated that three women came to him with the blanks for him to sign, applying for aid, who, so far as he knew were perfectly able to pay for the maternity care. He said he did not see why a doctor could not get \$50 or more for taking care of the patient, and not have to accept \$35 from the Government. For these reasons, Dr. Smith said, the Nashua Medical Society, not an official body, so far as the New Hampshire Medical Society was concerned, voted to disapprove the plan.

The meeting then adjourned at 10:30 p.m. until 8:30 a.m., May 11.

The House of Delegates convened at the Hotel Carpenter, Manchester, on May 11, 1943, at 8:30 a.m., with Speaker Charles H. Parsons, of Concord, presiding.

The following members answered the roll call:

The President, *ex-officio*
 The Vice-President, *ex-officio*
 The Secretary-Treasurer, *ex-officio*
 W. J. Paul Dye, Wolfeboro
 Francis J. C. Dube, Center Ossipee
 Walter F. Taylor, Keene
 A. C. Johnston, Keene (alternate for Norris H. Robertson)
 Leander P. Beaudoin, Berlin
 Arthur B. Sharples, Groveton
 Arthur W. Burnham, Lebanon
 Leslie K. Sycamore, Hanover
 Deering G. Smith, Nashua
 Edward V. Putnam, Warner
 Clarence E. Butterfield, Concord
 Frederick S. Gray, Portsmouth
 Anthony E. Peters, Portsmouth
 Edwin D. Lee, Exeter
 Roland J. Bennett, Dover
 George G. McGregor, Durham
 B. Read Lewin, Claremont
 Emery M. Fitch, Claremont (alternate for Henry C. Sanders, Jr.)

Dr. Putnam presented a report, held over from the day before, on the National Conference for Medical Service. He explained that in conference with some of the other delegates, it had been decided that the basic point seemed to be a question of some sort of liaison officer or commission to be established in Washington for the purpose of mak-

The report was accepted. Dr. James W. Jamieson, of Concord, was elected president, and Dr. Fred Fernald, of Nottingham, was elected vice-president. The Secretary was instructed to cast one ballot for the remainder of officers and committee members, as nominated; this was done, and all were declared duly elected.

Dr. Metcalf moved a vote of gratitude to the members in Manchester who had arranged the details of the meeting; it was so voted.

Under unfinished business Dr. McGregor opened discussion about maternity fees for soldiers' wives, in order to see if there was some way in which the fee schedule could be increased, and to ascertain what fees were being paid in other states. There seemed to be considerable misunderstanding as to whether the agency concerned was a Government or a Red Cross agency. Some doctors were not satisfied with the present fee schedules. The amount did not seem to meet the minimum for the hospital in Exeter.

Dr. Sycamore thought that this question called for more investigation by the Committee on Maternity and Infancy, and added the matter could be left in their hands to make alterations, if possible.

Dr. D. G. Smith spoke as follows:

I believed that Dr. Burpee would tell more about the plan than he did. It was brought to my attention first about ten days ago. I got the feeling that the thing was rushed through, perhaps slipped through rather rapidly, because there was a copy of a letter sent to the Red Cross in Nashua that was to be sent to every doctor in the State. I, for one, did not receive the letter. I have talked to a number of others who received no letter explaining the plan. The fee list was apparently established by Dr. Burpee — because Dr. Fairfield was on the same committee with Dr. Burpee and said they were consulted — and was rather hurriedly adopted. That was probably why the medical society was not consulted.

A number of men in Nashua think this is an entering wedge for state medicine; that the Government is appropriating this money to the State Board of Health and the Children's Bureau, dictating our fees. They say if the Government is starting now to take care of the soldiers' wives and children, it will be only a short time after the war when they are taking care of the soldiers. The doctors in Nashua are opposed to it. Also, they did not think that the fee schedule is high enough.

Speaking unofficially, in talking with the Superintendent of the Memorial Hospital in Nashua, I discovered that \$45 for ten days would not cover the cost of hospital care. It would not take care of a number of things, such as charges for x-ray films, delivery room, medicines, anesthesia, supplies and what not, including care of the baby, and it was said last night

that the doctors there are very much opposed to the general idea. Probably we can do little or nothing about it, but the men are especially upset about the dictation as to the fees. It is bad enough on welfare cases, but why should they be dictated to us on other cases? Many of these people have sufficient funds to pay these bills.

The original appropriation, according to Dr. Chamberlain and the head of the Red Cross in New Hampshire, was for the care of soldiers' wives who had no available funds, and this new appropriation is to take care of all soldiers' wives in the four lowest pay groups, regardless of their income.

Dr. Gray said he thought that a discussion of the fee schedules should be carried on by the committee, as previously suggested, and that the House of Delegates should go on record as recommending that an elastic fee schedule be adopted, or at least recommended, whereby in abnormal cases, a higher fee could be charged, and that the top limit be not set as it is in the recommendation.

Dr. Smith said that an alternative proposal was made by Dr. Fairfield, namely, that a grant of \$35 toward the doctor's bill and \$45 toward the hospital bill be given to the soldiers' wives, if they needed it, and that the balance be taken care of by the individual. He moved that the delegates go on record as being opposed to the present fee schedule for the maternity care of soldiers' wives as inadequate, and as suggesting to the committee that either these rates be raised, or else the \$35 to be given to the doctor be considered as a part payment in some cases, and that the doctor be allowed to charge a reasonable balance. The motion was carried.

Dr. Dye, referring to the motion made the previous evening for expediting the medical insurance plan, asked for clarification of how the matter now stood. It was voted then that the Committee on Medical Economics and the officers be a committee to formulate a plan and to present such a plan at the earliest possible moment to the House of Delegates. Was there, he asked, a further provision that this plan be sent to each member of the House prior to said meeting, so that the members could look it over and discuss the question intelligently?

Speaker Parsons replied that no definite motion was made that that plan be specifically referred to each member, but it was understood that it would be; otherwise, it would be impossible to consider the matter intelligently.

The second and final meeting of the House of Delegates was adjourned at 9:15 a.m.

CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**BENJAMIN CASTLEMAN, M.D., *Acting Editor*EDITH E. PARRIS, *Assistant Editor*

CASE 29391

PRESENTATION OF CASE

A twenty-seven-year-old medical student was admitted to the hospital because of massive bloody stools.

The patient was in good health until two days prior to entry when he developed coryza, photophobia and slight sore throat. There was no muscle pain or stiffness. His bowels, which had moved normally the day before, had not moved on that day. The following day, while on a train, he noted that he was sweating more than usual and felt chilly. He had marked tenesmus with two unsuccessful attempts to pass a stool. The third time there was a pinkish spotting of the toilet. He felt weak and faint. About midnight that evening, two hours before entry, he had a great desire to defecate, broke out in a cold sweat and had a massive liquid, tarry and bloody, foul-smelling stool, with a volume of about "1½ to 2 pints." He felt weak and nauseated and vomited a yellow mucoid material in which no coffee grounds or blood was seen. He had had no pain, chills, fever, jaundice or other gastrointestinal or genitourinary symptoms. The upper respiratory infection was still present.

His appetite had always been good, and his weight steady. He had a "softening of the spine" at eighteen, for which he wore a brace for three months. Following a maxillary sinus operation, two and a half years before entry, he had had a tarry stool, but he had experienced no other episodes of melena until his present illness. There was no history of cough, night sweats, chest pain, hemoptysis, dyspnea, orthopnea or heartburn.

Physical examination showed a well-developed, well-nourished man in no distress. The chest was somewhat barrel shaped and hyperresonant. The abdomen was scaphoid, entirely soft and nontender. Peristalsis was normal. The liver edge could be felt and percussed two fingerbreadths below the costal margin in the anterior axillary line. Rectal examination showed some tarry material on the examining finger.

on face of observer

The blood pressure was 90 systolic, 70 diastolic. The temperature was 99°F., the pulse 96, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,150,000 and a white-cell count of 11,700. The blood protein was 5.4 gm. per 100 cc., the chloride 92.6 milliequiv. per liter. The prothrombin time was 22 seconds (normal, 20 seconds), and the hematocrit was 31 per cent. The urine was normal. The stools gave a +++ test for guaiac. The aspirated gastric content had free hydrochloric acid and was guaiac negative.

During the physical examination, shortly after admission, he had two large, loose, foul stools of tarry material admixed with red blood. He became pale and felt faint. He was given 1000 cc. of whole blood intravenously. The bleeding subsided, with elevation of the blood pressure.

The following day, the bleeding having ceased, a gastrointestinal series was done. This showed a normal esophagus, and there was no evidence of a hiatus hernia; the stomach and duodenal bulb were normal.

The third day, when plans were being made for further study, the patient had another massive, grossly bloody stool and showed "early evidence of shock." An abdominal exploration was performed immediately.

DIFFERENTIAL DIAGNOSIS

DR. ROBERT R. LINTON: We have a history of a twenty-seven-year-old, apparently healthy young man who suddenly developed massive bleeding in the rectum. The bleeding consisted not entirely of old blood, characterized by tarry material, but also of some fresh blood. The first thing one thinks of, of course, is a bleeding duodenal ulcer. There usually is no fresh blood in the stools following bleeding from a duodenal ulcer, but on the other hand it may occur. It is true that he had no history of previous ulcer symptoms, and there is nothing to suggest that he had a duodenal ulcer; nevertheless, duodenal ulcers may suddenly bleed or perforate without any preliminary symptoms suggestive of the disease.

The physicians looking after this patient seem to me to have been courageous in giving a gastrointestinal series the morning following so much bleeding. This may have been all right, but it is not the way we have been taught to handle massive hemorrhage supposedly from duodenal ulcer. They may have thought of some other diagnosis and felt free to go ahead. At any rate, their judgment was correct, since there was obviously no lesion involving the stomach or duodenum. At the same time they ruled out esophageal varices, which one would have to consider as a possible diagnosis.

The likelihood that there were esophageal varices is very small because of the fact that there was no vomiting of blood, which practically always occurs if there is bleeding from this source. It seems to me that one has to accept the x-ray report that there was nothing wrong with the stomach and duodenum, so that the bleeding did not come from high in the gastrointestinal tract.

What other conditions can produce massive bleeding? I suppose that a tumor of the jejunum is a possibility. Tumors of the jejunum are rare. I have never happened to see one that bled so much as this one did, and usually intestinal obstruction is associated with it, which this man did not have. So I do not see how we can incriminate

of bloody material. So I do not believe that he had an intussusception or carcinoma of the colon, with bleeding from either of these conditions. Lymphoma is another cause one must consider. Because the stool contained old and fresh blood I should expect such a lesion to be in the terminal ileum or the right colon. Other conditions that I have read about but have not seen, such as congenital hemangioma involving some part of the gastrointestinal tract, may cause bleeding. If that is what it is, the diagnosis would be purely a guess on my part, and for that reason I am going to rule it out in the differential diagnosis.

In reviewing this case it seems to me that, since the gastrointestinal series was negative and since

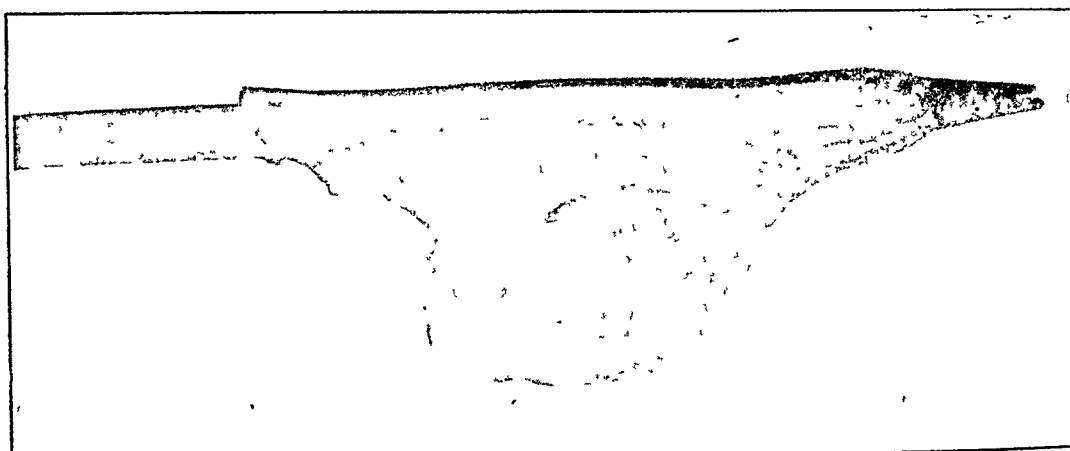


FIGURE 1.

the jejunum. Then we come down farther to the ileum, where one must consider two conditions seriously—intussusception and a Meckel's diverticulum. Intussusception is unusual in a man of twenty-seven. It usually occurs in infants and in children under five; there was also too much bleeding for intussusception. Bleeding from an ulcer in a Meckel's diverticulum again is unusual in a patient of twenty-seven. Such lesions do occur, however, at that age but are much commoner under the age of ten. The other conditions that we should consider are carcinomas involving the large bowel. The cecum, for instance, is a common site for bleeding from the rectum; but again, massive hemorrhage from tumors in the cecum usually does not occur: it is usually a continued, small amount of bleeding. The same is true of carcinoma of the colon, in which one observes less bleeding than in carcinoma of the cecum. The history is of interest in that it states that the patient had marked tenesmus with two unsuccessful attempts to pass a stool, which suggests that he had some degree of intestinal obstruction. Apparently this did not amount to much because within a few hours he did defecate a large amount

the patient passed large amounts of blood that was both old and fresh, indicating that the hemorrhage arose somewhere in the middle of the intestinal tract rather than at either end of it, and since the lesion was asymptomatic in that he had had no preliminary gastrointestinal symptoms previous to this episode except for the one time after the sinus operation when he passed some blood by rectum, I am going to make a diagnosis of an ulcer in a Meckel's diverticulum. A Meckel's diverticulum is usually asymptomatic unless it produces signs of intestinal obstruction, becomes acutely inflamed or develops an ulcer, which erodes a blood vessel and produces bleeding similar to that of a duodenal ulcer. The ulcer that forms is secondary to the fact that some of them contain gastric mucosa, which secretes hydrochloric acid. Since the mucosa of the ileum has no neutralizing secretion against this acid, it is apt to produce an ulceration similar to that of peptic ulcer, either at the base of the diverticulum or in the adjacent ileum.

DR. JOSEPH C. AUB: Would Dr. Linton consider the possibility of "walking" typhoid fever? He was a medical student and had been miserable for two days.

DR. LINTON: It was my impression that cases of typhoid fever do not bleed. They perforate, but do not bleed.

DR. AUB: They sometimes bleed.

DR. J. H. MEANS: I should like to mention one patient who had a massive gastrointestinal hemorrhage, the source of which was not found until operation. He had gastric varices without esophageal varices. They did not show in the x-ray; in fact they were not seen at gastroscopy.

DR. BENJAMIN CASTLEMAN: Is it not true that the patient had appreciable symptoms before the bleeding?

DR. MEANS: Yes. Such a diagnosis is most unlikely, but if you are considering all the possible explanations that might be mentioned.

DR. LINTON: I may be making a mistake by passing over the diagnosis of duodenal ulcer, but on the other hand this seems to be a very unusual case and is more likely to have been due to something lower in the gastrointestinal tract.

DR. FRANCIS D. MOORE: How about polyposis of the colon?

DR. LINTON: That is a possibility. However, I should not expect the bleeding to be so massive.

DR. MOORE: On the service we followed much the same reasoning that Dr. Linton has. We knew that this man might start to bleed massively again, which would necessitate operation. If we did operate, we wanted to locate the lesion, if possible. That is why we asked for the gastrointestinal series, although we realized that it carried some hazards. When he started to bleed again, we operated through a lower abdominal midline incision and immediately saw blood in the small bowel. This confirmed our suspicion that the blood was coming from above the ileocecal valve, and we shortly found that it was emanating from a tumor in the ileum in the region where one expects to find a Meckel's diverticulum. The tumor was about the size of a lemon, and we thought that it was associated with a Meckel's diverticulum. The tumor was resected, and the patient has done extremely well.

CLINICAL DIAGNOSIS

Meckel's diverticulum, with ulcer.

DR. LINTON'S DIAGNOSIS

Meckel's diverticulum, with bleeding ulcer.

ANATOMICAL DIAGNOSIS

Neurofibroma of ileum.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: This is a photograph of the specimen (Fig. 1), showing the tumor through the

serosa. It was a lobulated, soft, somewhat gelatinous intramural tumor about 5 cm. in diameter. There was no Meckel's diverticulum. The usual benign intramural tumors of the gastrointestinal tract are the leiomyomas and neurofibromas; the malignant ones are the leiomyosarcomas, neurogenic fibrosarcomas and lymphomas. This one proved to be a neurofibroma. These tumors usually ulcerate in the center and often produce massive bleeding.

DR. LINTON: Did you find the bleeding point?

DR. CASTLEMAN: We did not find the bleeding point. The specimen was already sectioned when received in the laboratory.

DR. MOORE: After taking a picture of the specimen we opened it and found the bleeding point to be a dilated vein about twice the size of the lead of a pencil. Where the tumor was close to the mucosa the vein had ruptured into the lumen of the bowel.

CASE 29392

PRESENTATION OF CASE

A forty-five-year-old housewife was admitted to the hospital about midnight because of severe abdominal pain. The patient was too sick to give a complete history.

About thirteen hours before admission, soon after lunch, the patient developed severe pain in the upper abdomen and back, associated with nausea and vomiting. That evening, while visiting her husband, who was in a hospital, she collapsed. She was seen by a physician who sent her to this hospital.

For the past twenty-five years she apparently had had recurrent attacks of pain in the upper abdomen, associated with nausea and vomiting, which had been interpreted as being due to gallstone colic.

Physical examination showed a lethargic, ill-appearing, moderately obese woman, complaining of pain in the upper abdomen. The skin was moist. There was questionable jaundice of the skin and scleras. There was an apical systolic murmur, but the heart was otherwise normal. The lungs were clear. There were spasm, resistance and a sense of a mass in the right upper quadrant, with tenderness in the right lower quadrant, the left upper quadrant and the left costovertebral angle. Peristaltic activity was somewhat reduced but essentially normal. There was a suprapubic abdominal mass that was more prominent on the right than on the left and still present after catheterization. On vaginal examination this mass was believed to be a fibroid uterus.

The blood pressure was not obtained. The temperature was 99°F., and the pulse 100; the respirations were normal.

Examination of the blood revealed a hemoglobin of 18.7 gm., and a white-cell count of 9200. The urine was dark amber, cloudy and acid, with a specific gravity of 1.019 and a +++ test for albumin and bile. The sediment contained many granular, hyaline and cellular casts, and occasional red cells, 10 white cells and 20 epithelial cells per high-power field. A urine culture was negative.

An x-ray film of the abdomen showed both kidneys to be normal in size, shape and position. There were several areas of calcification having the appearance of calcified lymph nodes near the right transverse processes of the third lumbar vertebra. No shadows suggesting renal or ureteral stones were seen. There were no dilated loops of small bowel. Films taken in the upright position showed no air under the diaphragm.

Ten hours after admission an exploratory laparotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD H. SWEET: In this patient, the onset was acute, the story short and the illness severe, the outstanding symptoms being abdominal pain going through to the back, and nausea with vomiting, the collapse following later. In the past history we learn that for twenty-five years she had had recurrent attacks of upper abdominal pain associated with nausea and vomiting, which had been interpreted as being due to gallstone colic, but I am sure you are all acquainted with the fact that nausea, or at least vomiting, is not an outstanding symptom of the ordinary uncomplicated gallstone attack. Very frequently we see gallstone colic without any vomiting. This patient, however, had vomiting with all the attacks.

In a physical examination made at about 1:00 a.m., I think that most of us would find it difficult to decide whether the patient was jaundiced; so I do not attach much significance to that finding until later when we discover that she had a large amount of bile in the urine.

It is interesting that this patient had widespread tenderness; in fact the only place she did not have any was in the left lower quadrant. Thirteen or more hours after the sudden onset of the abdominal pain and the pain in the back, there were marked physical findings related entirely to the abdomen. In fact the tenderness was so widespread that it suggests peritonitis. The maximal tenderness and spasm were in the right upper quadrant.

The blood pressure is not recorded. It might have been of some help.

The white-cell count was low for a person as ill as this, provided she had an inflammatory process. The hemoglobin indicates that she had not been suffering from blood loss. Since the urine gave a +++ test for bile, its presence cannot be doubted. I presume that the specimen was voided; hence the few red cells, the 10 white cells and 20 epithelial cells have little or no significance.

Whoever saw this patient thought of a perforated ulcer and had an abdominal film taken in the upright position, which did not show any gas under the diaphragm. Although, of course, there are plenty of cases in which this does not occur, the presumption is that we are not dealing with a case of perforated ulcer. Furthermore, the attacks of upper abdominal pain that the patient had had for twenty-five years do not sound like those due to ulcer. The physician in charge of the patient also thought of small-bowel obstruction, but there were no dilated loops.

I presume that renal or ureteral disease was considered as well. All abdominal surgeons have at times seen people with renal or ureteral disease, caused by stone or infection, in whom the spasm and tenderness and the superficial behavior were such that a diagnosis of peritonitis was made. I remember being called one night to see a patient at the Deaconess Hospital. The medical man said, "This girl has peritonitis and something should be done about it." The abdomen was so spastic that it was boardlike, and yet there were perfectly normal peristaltic sounds. She had an acute renal shutoff, with secondary infection and fever. I presume, however, that this is not a case of renal or ureteral disease. There was no x-ray suggestion of a stone, although, of course, it might not have been visible. A report on a catheter specimen of urine would be helpful.

May we see the x-ray films?

DR. MILFORD D. SCHULZ: These films show no evidence of gas in the peritoneal cavity. There are calcified mesenteric lymph nodes. I see no evidence of biliary or renal calculi. The preperitoneal fat line seems to be preserved. If she had a localized peritonitis it could not have been of long standing.

DR. SWEET: This patient did not behave the way patients with perforated ulcer usually do. She had pain but was still well enough early that evening to visit her husband, who was in a hospital. If it was a perforated ulcer, there must have been a tiny leak that became temporarily sealed off, so that she was able to walk about for five or six hours, and then underwent a massive rupture, which produced collapse. This is a possibility, but a rather unusual one, I should say.

Was this an ordinary attack of gallstone colic? I do not believe so. Of course some people react

to pain much more severely than others, and I presume that the collapse occurred because the patient was suffering a terrific amount of pain. We do not know what the blood pressure was. I assume from the description, however, that she really was in collapse. Because of the fact that nausea and vomiting were outstanding symptoms, I shall exclude gallstones as the immediate cause of the difficulty. I shall also exclude acute cholecystitis because she had an essentially normal temperature and a normal white cell count after thirteen hours. Acute cholecystitis, as you all realize, is one of the few conditions that will cause excessively high white cell counts, sometimes quite early in the course of the disease.

Could she have something related to the intestinal tract other than perforation of an ulcer? We cannot exclude small bowel obstruction, even in the absence of dilated loops by x-ray, but it would be most unusual for this condition to produce pain of this severity and lead to sudden collapse of the patient. I shall exclude it.

How about mesenteric thrombosis? The patient was rather young. Furthermore, most of the cases usually have a very high white cell count, and the pain is not quite typical.

There is one acute abdominal emergency that I have not touched on which fits the whole picture and even ties in with the history of gallstone attacks—namely, acute pancreatitis. A prodromal attack of pain is characteristic. The pain in pancreatitis is always upper abdominal, and it frequently goes to the back. A great many patients complaining more of pain in the back than anything else. Most of the patients with pancreatitis whom I have seen would not be described as lethargic early in the course of the disease; they are apt to be writhing in bed, complaining of pain in the back and upper abdomen. The white cell count is not inconsistent; patients with acute pancreatitis often have relatively low counts, and early in the disease they often have low temperatures. The physical examination is consistent with acute pancreatitis—namely, tenderness in the left upper quadrant, right upper quadrant and right lower quadrant.

I have not considered acute appendicitis because the onset was severer than one would expect in that condition. Furthermore, the distribution of the tenderness as well as the maximal tenderness in the upper rather than in the lower abdomen, seems to exclude it.

For reasons mentioned before, I have excluded intraabdominal hemorrhage from such conditions as ruptured ectopic pregnancy and accident connected with an abdominal pelvic tumor, such as rupture of a cyst. So with the history as given

and with the physical signs as stated, I shall incline toward a diagnosis of acute pancreatitis to explain the present illness. On the basis of the past history we must also conclude that she had cholelithiasis.

CLINICAL DIAGNOSIS

Acute pancreatitis

DR SWEET'S DIAGNOSES

Acute pancreatitis

Cholelithiasis

ANATOMICAL DIAGNOSES

Acute hemorrhagic pancreatitis

Cholelithiasis

Cholelithiasis

PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMAN: At operation the surgeon found a distended gall bladder, to which the omentum was adherent. He inserted a trocar into the gall bladder, and some light colored bile came out. He was able to scoop out several stones from the cystic duct, following which the bile became normal in color. The peritoneal cavity contained slightly blood tinged fluid and several small areas of fat necrosis. He believed that the patient was too sick to do anything more. A drainage tube was placed in the gall bladder. The patient died a few hours later.

At autopsy we found an extensive hemorrhagic pancreatitis. The whole pancreas was involved, and there were areas of fat necrosis throughout the omentum and peritoneum. The cystic duct was markedly thickened and dilated and contained numerous stones, which apparently the surgeon was unable to remove. The common duct was also thickened and markedly dilated and was filled with faceted stones along its entire course. Stones were also present in the intrapancreatic ducts.

In this case I am sure that the cause of the pancreatitis was a blockage of the exit of bile, with bile entering the pancreatic duct. It is satisfying to have a case of acute pancreatitis in which we are able to determine the exact cause, in many cases we find no stones or other cause for the pancreatitis. There is no squamous cell metaplasia of the epithelium of the pancreatic ducts.

DR EDWARD B. BENEDICT: Do you mean that pancreatitis without any gall bladder disease occurs in a great many cases?

DR SWEET: The late Dr Daniel F. Jones* looked that up some years ago and found that 40 per cent of the cases occurred in the absence of stones.

* Jones D. F. Acute pancreatitis. *Bull. on Med. & S.* 186 33 342 192

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BY THEIR FRUITS—

THE time has come when the Victory Gardener, at long last, can count his chips and see if the game he has been playing this departed summer has gone for him, or against him. Discounting the element of luck, present in all our enterprises in inverse proportion to the amount of time spent in planning and in executing our plans, he should be able to mark up a good score against his opponents in the game—poor soil, pests and plant disease, weeds, drought and indolence. Of these the last, perhaps, is the most important. Many an inspired spring planter has found his enthusiasm wilting under a July sun and the

necessity for regular cultivating, weeding, spraying, dusting and watering.

The number of seeds that have gone into the ground this planting season must certainly have been astronomical; Nature herself rings the bell on too gross overproduction, else we might be reminded of the geometric computation concerning the fly's eggs: If every egg hatched and produced a fly and these flies' eggs hatched and produced flies, and so on through the creatures' generations, how large would the resulting fly mass be in a specified time? Instead we are reminded of the parable of the sower, or perhaps, facetiously, of Jack Benny's description of his potato crop—some were the size of marbles, some were as big as peas, and there were quite a number of small ones

Be their productive ratio as it may, the number of war gardens that have burst into being in the backyards and waste spaces of America, when properly cultivated and harvested, must add an appreciable increment to our precarious food supply. They have done more than that; they have drawn many thousands of indoor workers into the most healthful recreation known, but none, and have added greatly to hundreds of thousands of individuals' previously meager knowledge of the methods of production and relative values of the various vegetable foods.

Fortunately for us, information on gardening and on the storing of crops has been freely available. It is essential, however, that the latter should be properly carried out. Short cuts and slipshod methods in the preserving of vegetables and fruits, particularly in home canning, may lead to serious dangers, as has been indicated in Dr. Getting's^{*} excellent and timely articles in recent issues of the *Journal*. Although botulism is relatively uncommon in the East, it is by no means unknown and is usually the result of the underprocessing of nonacid foods. Foods put up at home by the cold-pack method should be reboiled for ten to fifteen minutes after opening and before eating

*Getting, V. A. Epidemiologic aspects of food borne disease. *J. Med.* 2:8 754 762 788 796 and 823 830 1943

or tasting. The much commoner staphylococcal enterotoxin is heat stable, but is much likelier to be found in canned foods that have spoiled after opening than to have survived ordinary processing.

SEVENTY-FIVE YEARS OF ACHIEVEMENT

THE Metropolitan Life Insurance Company celebrated its seventy-fifth anniversary last spring. Founded in March, 1868, it has witnessed the greatest period of progress in public health that the world has ever seen and has, particularly in the latter half of the period, been a factor in carrying on and in helping to initiate many of these advances. In the *Statistical Bulletin* for March, 1943,—an anniversary number,—the company has reviewed these seventy-five years of progress.

In 1868 the death rate for New York City was 28 per 1000 persons, reaching 40 in some wards, and even higher figures in individual blocks. As a result of this high mortality, particularly among children, the average length of life was correspondingly low—about forty years, as against sixty-four years today. In the underprivileged classes of society worse than the average conditions prevailed.

Public-health organizations, however, soon began to put into effect the knowledge gained from the discoveries of Pasteur and the experiments of Lister, and although gains were at first slow, medical progress really began to hit its stride with the turn of the century. In 1909 the company launched an organized welfare program, and from that time on its health program, combining nursing and educational activities among policyholders with co-operation and support of existing health organizations, has been identified with most of the health advances made in this country and Canada.

The statistical experience among industrial policyholders of the company exemplifies the progress that has been made. In 1911 the standardized death rate from all causes among these policyholders between the ages of one to seventy-four was 13.5 per 1000, whereas in 1942 it was 6.1. During the same period the average length of life in the group has increased from less than forty-seven years to about sixty-four years. The infant death rate has dropped to about one fifth of its 1920 figure; the mortality in the age group from one to fourteen has improved four fifths since 1911; tuberculosis, with a death rate of more than 220 per 100,000 in 1911, has now a rate of scarcely more than 40; and between the years 1937 and 1941, the mortality from pneumonia has been reduced by 54 per cent. The current death rate from appendicitis is the lowest in history; and the mortality from all accidents, even including those due to automobiles, has been reduced. In fact, if war could be banished, one might say that the people of this country alone were facing a millennium.

The activities of the welfare program deserve a brief review. Most vital has been a nursing service to policyholders, now reaching nearly eight thousand communities. In the field of health education, about one and a quarter billion pamphlets have been distributed, and the company's motion pictures have been viewed by more than one hundred and twenty-five million persons. The well-known demonstration at Framingham, Mass., showed how a community could solve its tuberculosis problem; the demonstration at Thetford Mines, Quebec, reduced infant mortality by two thirds in three years; and important advances in the treatment of pneumonia have been aided by the Influenza-Pneumonia Commission, organized in 1919.

Its seventy-five years of achievement have certainly justified the high respect in which this organization is universally held.

MEDICAL EPONYM

GILBERT'S DISEASE

This was first described by Professor A. Gilbert (1858-1927) at a meeting of the Société médicale des hôpitaux de Paris on July 27, 1900, in a paper entitled "De l'ictère familial: contribution a l'étude de la diathese biliaire [Familial Jaundice: A contribution to the study of the biliary diathesis]," in collaboration with Drs. J. Castaigne and P. Lereboullet, in which a number of cases of jaundice of diverse origin are described. Their paper appeared in *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* (17:948-959, 1900). A portion of the translation follows:

Whatever else the nature of this hereditary predisposition to infection of the biliary passages may be, it seems to us to be proved by the facts that we have reported. Not only lithogenic angiocholecystitis, then, is hereditary; simple or cirrhotogenous angiocholitis may equally be so, and by reason of this predisposition, one may meet in a single family with the various clinical types, the principal characteristics of which we have described.

In subsequent papers he further describes simple, nonhemolytic familial jaundice—for example in an article entitled "La cholémie simple familiale [Simple Familial Cholemia]," in the *Gazette hebdomadaire de médecine et de chirurgie* (7:889-897, 1902) he states: "Familial cholemia is extremely common. . . . It is a familial, hereditary disease."

R. W. B.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR AUGUST, 1943

Résumé

DISEASES	AUGUST 1943	AUGUST 1942	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	24	2	9
Chicken pox	123	121	118
Diphtheria	7	12	12
Dog bite	1093	1031	1068
Dysentery, bacillary	14	4	15
German measles	72	83	31
Gonorrhea	374	479	433
Measles	346	296	281
Meningitis, meningococcal	42	18	4
Meningitis, other forms	5	1	•
Meningitis, undetermined	4	1	•
Mumps	137	271	157
Pneumonia, lobar	76	121	120
Salmonella infections	22	13	16
Scarlet fever	250	224	125
Syphilis	418	354	367
Tuberculosis, pulmonary	274	265	289
Tuberculosis, other forms	25	19	27
Typhoid fever	3	9	11
Undulant fever	5	4	4
Whooping cough	286	673	533

*Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

COMMENT

The poliomyelitis situation in Massachusetts is of special interest at the present moment owing to the relatively large number of cases occurring in certain other states. The incidence in August was about two and a half times the seven-year median, and subsequent weeks will probably show a still further increase. Nevertheless, the season during which poliomyelitis usually occurs is now so far advanced that the chances are against the occurrence of a real epidemic this year.

Meningococcal meningitis has shown the seasonal decline that was expected, although the level is higher than in the average year. The August figures are less than half those of June. Salmonella infections, on the other hand, show an increase over those of the last three months. These were distributed through eleven towns and do not represent any major outbreak.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Arlington, 1; Attleboro, 3; Beverly, 1; Boston, 1; Braintree, 1; Brockton, 1; Cambridge, 1; Chelsea, 1; East Longmeadow, 1; Everett, 1; Fall River, 1; Lynn, 1; Marblehead, 1; Medford, 1; New Bedford, 2; New Marlboro, 1; Norton, 1; Palmer, 1; Quincy, 2; Waltham, 1; total, 24.

Anthrax was reported from: Woburn, 1; total, 1.

Diphtheria was reported from: Amesbury, 1; Athol, 2; Dighton, 1; Somerville, 2; Westport, 1; total, 7.

Dysentery, bacillary, was reported from: Boston, 1; Chelsea, 3; Holyoke, 9; Worcester, 1; total, 14.

Encephalitis, infectious, was reported from: Everett, 1; total, 1.

Malaria was reported from: Boston, 1; Chicopee, 1; Concord, 1; Fort Banks, 4; Fort Devens, 5; Milford, 1; Springfield, 1; total, 14.

Meningitis, meningococcal, was reported from: Athol, 1; Attleboro, 1; Barnstable, 1; Boston, 6; Brookline, 1; Bridgewater, 2; Camp Edwards, 4; Chelmsford, 1; Chelsea, 1; Everett, 1; Fitchburg, 1; Fort Devens, 2; Gloucester, 1; Holbrook, 1; Holyoke, 2; Lawrence, 2; Longmeadow, 1; Lowell, 2; Lynn, 2; Malden, 1; Medford, 1; Middleboro, 1; Montague, 1; Southbridge, 1; Swampscott, 1; Taunton, 2; Weymouth, 1; total, 42.

Meningitis, other forms, was reported from: Foxboro, 1; Malden, 1; Pittsfield, 1; Springfield, 2; total, 5.

Meningitis, undetermined, was reported from: Boston, 1; Springfield, 1; Worcester, 2; total, 4.

Salmonella infections were reported from: Adams, 1; Beverly, 2; Everett, 1; Haverhill, 4; Marblehead, 3; Melrose, 1; Northfield, 5; Salem, 2; Somerville, 1; Winchester, 1; Worcester, 1; total, 22.

Septic sore throat was reported from: Boston, 5; Pittsfield, 1; total, 6.

Tetanus was reported from: Foxboro, 1; Falmouth, 1; Somerville, 1; total, 3.

Typhoid fever was reported from: Ludlow, 1; Shirley, 1; North Adams, 1; total, 3.

Undulant fever was reported from: Adams, 1; Brookline, 1; Hopkinton, 1; Lowell, 1; Whitman, 1; total, 5.

CONSULTATION CLINICS
OR CRIPPLED CHILDREN

CLINIC	DATE	CLINIC CONSULTANT
Lowell	October 1	Albert H Brewster
Salem	October 4	Paul W Hugenberger
Haverhill	October 6	William T Green
Brockton	October 14	George W Van Gorder
Worcester	October 15	John W O'Meara
Pittsfield	October 20	Frank A Slowick
Springfield	October 22	Garry deN Hough, Jr
Fall River	October 25	Eugene A McCarthy
Hyannis	October 26	Paul L Norton

BOOK REVIEWS

Clinical Laboratory Diagnosis By Samuel A Levinson
MD and Robert P MacL'ate, Ch E, MS Ph D Second
edition 8", cloth, 980 pp, with 156 illustrations 92 ta-
bles and 15 plates Philadelphia Lea and Febiger, 1943
\$10.00

The second edition of this book lives up to the ex-
pressed purpose of the first edition, namely, to present to
the student, intern, practicing physician and technician a
available review of clinical laboratory diagnosis to meet
general needs

The subject matter has been brought up to date, new
has been added and the special appendix on the
course in clinical pathology at the University of Illinois
College of Medicine has been deleted to provide space
new items have been added relating to water metabolism
and acid base balance. Recent blood clinical methods for
the determination of ascorbic acid, the sulfonamides
fluocyanate, alkaline and acid phosphatase, amylase and
other substances are described. The chapter on hemato-
logy has been enlarged to make room for a discussion of
bone marrow findings, Rh factor, blood volume and other
items. The inclusion of chapters on water and milk
analysis and toxicology and legal medicine as well as
histological technic, skin tests and other biologic exam-
inations adds value in that in a single volume one has
at hand a ready reference book on virtually any type of
examination with which clinical laboratory diagnosis may
be concerned in its broadest scope. A brief and concise
review of pertinent anatomical physiologic and biochem-
ical considerations is of great value in illuminating the
background of the accumulation of knowledge that is to
be interpreted by means of findings obtained by specialized
technical procedures.

A separate section on laboratory methods in pediatric
procedure is cited as an example of the well planned ar-
rangement of subject matter, which offers ready access
to the source of the specific information one may be

Method described in blood clinical analysis make use
of procedures which, so far as possible can be adapted
for either colorimetric or photometric determinations.
The simplification and adaptation of methods is particu-
larly of advantage in these times when new apparatus is
often if not impossible, to obtain.

The chapter on bacteriology is arranged in an orderly
fashion. Bergey's nomenclature and classification are fol-
lowed. The description of appropriate methods to be
used in the bacteriologic examination of specific materials
is particularly valuable to the inexperienced technician.
The charts of the characteristics and classification of the
commoner bacteria are a useful feature.

It is interesting to note the complete exposition cover-
ing the function and examination of saliva and pathologic
conditions of the mouth. In this section, as well as those
on the stomach and intestines, are old and tried methods
of examination, which, although little used nowadays,
have their value.

In the chapter on immunology and serology, serologic
tests for syphilis include the Kolmer complement fixation
test, the Kahn precipitation test and the Kline micro-
scopic slide precipitation test. The reviewer believes that
the Hinton test deserves at least mention as an acceptable
serologic test for syphilis.

This comprehensive treatise is concise and clear in
structure and in detail. The charts, illustrations and
tables are well chosen for their purpose, and add much
to the general usefulness of the book. It is highly rec-
ommended to those for whom it was written—the stu-
dent, the intern, the practicing physician and the tech-
nician. In addition, it should be in the working library
of every clinical laboratory.

*Surgical Practice of the Lahey Clinic Boston Massachu-
setts* 8", cloth, 897 pp with 376 illustrations Philadel-
phia and London W B Saunders Company, 1941
\$10.00

In this volume are collected seventy eight papers by the
staff of the Lahey Clinic, Boston previously published in
American journals in the years 1937-1941. Nearly half
are from *Surgical Clinics of North America*. According
to the preface by Dr Lahey, it is a cross section of the
methods in use in his clinic, representing an attempt at
standardization, which he believes is largely responsible
for improved end results. Written by twenty two con-
tributors, the papers are necessarily of uneven merit.

Nine papers by Dr Lahey and collaborators on the thy-
roid gland are authoritative and one on esophageal diver-
ticula is based on his almost unique experience with
such lesions. Articles on laryngoscopy, empyema, pul-
monary lobectomy, branchial cysts and carcinoma of the
breast are routine descriptions of technic. Twenty one
contributions by Lahey, Cattel and their associates on the
stomach, duodenum, colon and rectum describe methods
that they have proved to be effective. It may be noted
that no mention is made of the Miller-Abbott tube, whose
advent bids fair to supplant some of the methods de-
scribed. Four papers on the bile duct are of routine na-
ture and four gynecologic topics, three on the kidney and
prostate and six on orthopedic subjects necessarily cover
but little of those fields. Two important and useful
groups are those by Horrax and Poppen on neurosurgery,
and ten papers by Sise and his collaborators on anesthesia—
two fields of comparatively recent development in which
the work of the Lahey Clinic has been conspicuous.

The illustrations are numerous, many of them excel-
lent but some of the line drawings are quite inadequate
and a few are positively misleading. It is regrettable to be
obliged to say that the literary quality of some of these
papers leaves much to be desired, and that proper editor-
ial supervision has not been exercised. There are in-
stances of clumsy phrasing in some of which apparently,
a meaning is expressed precisely the opposite to that in-
tended. Did space permit it would be informative to in-
experienced writers to list these solecisms. A few are as
follows: the malignancy is now given to the pathol-
ogist (p 460) the removal of a large portion
of malignancy (p 481), and the entire bone-
flap may be safely elevated if the staphylococci [sic]

been proved, and I doubt that they have had any foundation in fact.

At the board meetings, hearings are conducted to settle the guilt or innocence of registered physicians against whom complaints have been made, or who have been found guilty in the courts. The complaints are usually concerned with negligence or deceit. The doctors who have been found guilty in the courts are those who, in most cases, have violated the federal narcotic law or have performed criminal abortions.

If the doctor is found guilty, his license is suspended or revoked, according to the seriousness of the case. Most of the complaints are handled by the secretary, who decides, after a conference, either that the matter can be settled without a hearing before the full board or that the complaint is not worthy of a hearing.

Complaints against unregistered practitioners of medicine are many and varied; these are turned over to the State Police for investigation. The latter frequently make arrests; the culprits are tried and if found guilty are fined. All that we have to do is to testify that the accused is not registered to practice medicine in the Commonwealth.

One of the duties of the board is to introduce legislation considered essential to the elevation of the standards of the profession, and for the protection of the interests of the people of the Commonwealth. I believe that it is also the duty of the board to oppose legislation that it knows is detrimental to the advance of medicine and the maintenance of its standards.

I have found out during the past year that it is very important at public hearings before a legislative committee to have one's facts well in hand, to be able to present arguments concisely, and not to antagonize the members of the committee. It is of the greatest help to be able to talk to the members of the legislature who may be influential in passing or defeating the legislation. An eagle eye must be kept on the calendar so that important bills may not slip by without the knowledge of the medical profession. One antivivisection bill reached the governor's desk this year without any opposition's having been presented by the profession. Fortunately, in this case, the omission was discovered in time to organize protests that finally brought about the withdrawal of the bill. By hard work and long hours spent on the problems, and with complete co-operation with the Massachusetts Medical Society, the board has been able to defeat two dangerous nursing bills and two antivivisection bills, and now has a bill in committee to continue the control of approved medical schools in this state forever.

Since the process of introducing legislation or defeating unfavorable legislation is a matter that concerns the law, and since physicians are very busy at their daily tasks of caring for the sick, and since physicians generally abhor anything that has to do with politicians and their ways, I believe that it would be for the best interests of this society to employ a legislative counsel to assist the members of the Committee on Legislation and of the Board of Registration in Medicine with such problems. A well-known and astute lawyer who "knows his way around" would be of great help, and I am sure that he would meet with the approval of those legislators who are looking after the interests of the medical profession.

Once a doctor has been registered to practice medicine in this state, he may do so throughout his life unless he is found guilty of gross misconduct. It has been extremely humiliating for our office not to be able to furnish information to the Army, the Navy, the F.B.I., the Committee of Ethics and Discipline of the Massachusetts Medical Society, hospitals, civic groups and individuals concerning doctors whom we have registered. For a small fee and a few minutes' time on the part of the doctors we could make it possible to know the pertinent facts concerning every registered physician in the Commonwealth; every member of this society could have the list in his bookcase; he could be immediately aware of the presence of the unregistered practitioner in his community; and the office of the board could give fairly accurate information to the right people concerning physicians registered in Massachusetts. I have no doubt that this information would have been of considerable help to the various district committees of the Procurement and Assignment Service during the past two years. I am sure that if every registered doctor had to reregister every year on his birthday, the profession as a whole would be benefited. Such legislation has been of great value to the nurses and the dentists.

The secretary of the Board of Registration in Medicine is the chairman of the Approving Authority for Medical Schools; the other two members of that board are the commissioner of education and the commissioner of health. It is the task of the authority under the present law to inspect medical schools at the request of their trustees. As you very likely know, the present law requires that any young man entering medical school after January 1, 1941, must graduate from an approved school in order to be allowed to take the examination for registration in this state. Therefore, after January 1, 1945, the problem of the unapproved medical school in the Common-

wealth will disappear, and Massachusetts will rise to an even rank with the other states. This most excellent piece of legislation was made possible by the combined efforts of the members of this society, the Board of Registration in Medicine and interested legislators.

The failure of the Massachusetts General Court to enact this important legislation earlier produced many difficulties for this society, the medical profession generally and the Board of Registration in Medicine in particular. Although it will take many years to eliminate all the bad results of inferior medical education in Massachusetts, at least we have the pleasure of knowing that the situation is improving constantly and that hereafter we need not be ashamed of our state in this important matter.

The secretary of the Board of Registration in Medicine is also the secretary of the Board of Registration in Nursing, which comprises six physicians and nurses who are leaders in their respective fields, who must shape the destiny of nursing education in the Commonwealth. It is the duty of this board to examine candidates for registration in nursing who are the graduates of any one of the sixty-three approved schools in Massachusetts, and to register those from other states by reciprocity if they meet the educational requirements of our law. These women must be at least twenty-one years of age and must have attended a school of nursing for one thousand and ninety-five days. Here again, each member of the board writes, proctors and corrects his own examination, and the candidates are known only by numbers. Since one does not have to be a registered nurse to work at her profession in Massachusetts there is no monetary value attached to the certificate, and the difficulties met with in the medical profession are not encountered.

The Board of Registration in Nursing also examines those who wish to become licensed attendants. These women must be twenty years of age or over and must have attended a school for the training of practical nurses. After October, 1944, they must be graduated from an approved school for attendants before they can take the examination for a license. Last year we licensed by waiver and examination about 2000 of these valuable women.

The secretary of the Board of Registration in Medicine is also the secretary of the Approving Authority for Nursing Schools. This board is made up of men and women who are on the ad-

ministrative, executive or teaching staffs of hospitals or nursing schools. They are appointed by the Governor. It is the work of this board to determine the educational qualifications of the prospective nurse, the courses to be taught in the nursing schools and the qualifications of the teachers in the nursing schools. It must determine the quality of the schools in every respect. To inspect the sixty-three approved schools in this state, to help them with their various problems, to try to improve them and to make sure that the quality of our nurses is maintained at a high level are the duties of two supervising nurses employed by our office. These nurses are at the top of their profession, and the success or failure of the work of the approving authority rests, to a great extent, on their shoulders. During this emergency, when there is a shortage of nurses, the approving authority has attempted in every way possible within the law to increase the number of nurses and at the same time to maintain high standards. Their latest act has been to present legislation to the Governor for emergency action whereby nurses may become registered at the age of twenty instead of twenty-one and attendants at the age of nineteen instead of twenty. If this is done, more young women will go into nursing schools as soon as they finish high school, since they will not have to await their eighteenth birthday.

* * *

I have presented an outline of the work of the Board of Registration in Medicine, the Board of Registration in Nursing and their respective approving authorities. All these units are functioning under new laws that promise to work to the advantage of medicine and nursing in the Commonwealth and eventually to bring it into line with the states that have the highest standards. There is no doubt that all this will be to the best interests of the public when they need medical and nursing care. Personally, I have but one aim in all this work: to improve the conditions in private practice and in hospitals that affect the care of patients. Better schools of medicine and nursing mean better physicians and nurses, and that means better care of the sick. The Board of Registration in Medicine is representative of the Massachusetts Medical Society. The board wants to do what you would like to have it do. We are trying at all times to interpret your desires to make the practice of medicine in Massachusetts the very best. We hope for, and expect to get, your co-operation in this vital work.

CARCINOMA OF THE LARYNX*

LEROY A. SCHALL, M.D.†

BOSTON

IT HAS been estimated that the larynx is involved in from 2 to 5 per cent of all cases of carcinoma. This incidence varies with different authors, since most of the data have been obtained from actuaries and are based on different opinions concerning the primary source of the tumor. Even acceptance of the lowest rate of incidence signifies that the disease is not uncommon. It has likewise been pointed out that the life expectancy in untreated cancer of the larynx is one year in 50 per cent of patients and that 95 per cent die within two years.

In no other internal organ of the body does cancer cause symptoms so early as it does when it occurs within the larynx. In the great majority of cases, laryngeal cancer begins as a lesion of the vocal cord. Here even a minute growth interferes with the normal function of the cord, and this interference is expressed as an alteration in the voice, progressing with time to a persistent hoarseness. Such hoarseness is so suggestive of something more serious than a simple laryngitis that the axiom, "In persistent hoarseness of two weeks' duration think of cancer, tuberculosis and syphilis," should never be forgotten.

Just as no other internal organ of the body produces a symptom so early as does cancer of the larynx, no other internal organ of the body can be so easily examined. In spite of these facts, it is not unusual to see not only patients with a history of hoarseness of months' and even years' duration who have received no medical advice, but also, and in too many cases, those who have been treated by gargles or sprays without the benefit of a laryngeal examination. Yet an examination of the larynx does not require unusual skill. A reflected light and a laryngeal mirror comprise the necessary equipment—and a few minutes of time.

In early laryngeal cancer the examination often reveals a proliferating new growth of the vocal cord and, in the vast majority of cases, it is the anterior half of the cord that is involved. Such a lesion is relatively benign; the lymphatics are few and scattered, so that the growth may persist for months and still be local. As the cancer slowly infiltrates along the long axis of the cord, it finally reaches the posterior half of the cord, where the lymphatics are more numerous, and from then on its progress is rapid. Fixation of the cord signifies

that the cancer has infiltrated through the mucous membrane into the muscle of the cord or into the cricoarytenoidal joint. It is no longer a lesion of the mucous membrane. From the posterior portion of the cord the cancer spreads to the subglottic space, into the ventricle, into the false cord, to the arytenoid and aryepiglottic fold, and frequently to the esophagus and to the cervical lymph nodes.

Laryngeal cancer that is untreated or that fails to respond to treatment terminates with extreme suffering and a lingering death. Laryngeal obstruction means a fight for air, relieved only by tracheotomy. Extension to the mouth of the esophagus blocks the lumen so that the patient drools, since he cannot swallow his own saliva. Gastrostomy for feeding is frequently necessary. Involvement of the superior laryngeal nerve means severe pain, frequently referred to the temporomandibular joint or to the ear.

Just as no other internal organ of the body produces so early a symptom as does the larynx in cancer, and just as no other internal organ is so easily examined, so in no other internal organ of the body does cancer present a larger series of cures than it does in the larynx.

The limits of time do not permit a detailed discussion of the treatment of laryngeal cancer. The selection of the treatment is a highly individual one, and no hard and fast rule can cover every case. The location of the growth, the extent of the lesion, the degree of malignancy and the degree of cord fixation, as well as the physical condition of the patient, should determine the plan of treatment.

The ideal treatment is one that not only eradicates the disease but also leaves a normal physiologic state. External irradiation answers these requirements. Laryngeal cancer that responds to irradiation leaves the patient with a normal, or nearly normal, useful voice.

Cancer of the larynx may be classified as follows: Group I—small localized lesions of the vocal cord; Group II—extensive cordal or subglottic intrinsic growths; and Group III—intrinsic involvement with extrinsic extension.

In Group I, the small localized cordal growths, irradiation is to be preferred if the cancer is of Grade III or IV according to Broder's classification, and surgery if it is of Grade I or II. Surgery has in its favor that it can be performed under

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local anesthesia; that the operative mortality is less than 1 per cent; that the period of hospitalization averages ten days to two weeks; and that unless the vocal process is removed there is frequently a regeneration of the vocal cord. When the case has been properly selected as suitable for laryngeal surgery by laryngofissure, a three-year to five-year cure can be obtained in approximately 75 to 82 per cent of cases, depending on the knowledge and skill of the operator.

In Group II, where there is cord involvement with subglottic extension, most radiologists agree that the carcinoma is not radiosensitive and that irradiation should not be used. Surgery offers only a total laryngectomy as a hope of cure.

In Group III, the extensive intrinsic and extrinsic carcinomas, particularly those of Grade III or IV, irradiation is the treatment of choice, although it may be only palliative.

The history of total laryngectomy is interesting. It is a little more than fifty years since Dr. J. Solis-Cohen,¹ assisted by Dr. W. W. Keen, operated on Daniel Hickey, performing the first successful total laryngectomy in the United States. Improvement in anesthesia as well as in surgical technic has robbed this operation of its high mortality. Among 53 patients, I have lost 2 from conditions attributable to the operation. One died from pneumonia on the sixth postoperative day, and the second from cardiac failure on the eighteenth postoperative day, on the eve of her discharge from the hospital.

From the earliest writings concerning cancer of the larynx to the most recent ones, total laryngectomy has often been described as a mutilating procedure leaving its victim in a pitiable condition—one that is worse than death. The psychic reaction to the loss of the power of speech, it is said, frequently leads to suicide or to insanity.

The medical profession and the public are familiar with the blind, the deaf and the crippled. Neither the public nor the vast majority of physicians are familiar with the patient who has lost his larynx and consequently the power of normal speech. It is a human failing to avoid the unknown. There is need of educating the medical profession as well as the laity to an understanding that the laryngectomized patient is not a pitiable creature who has given up all that life holds dear. It is hard properly to evaluate human suffering. The blind say that they would rather be blind than deaf; the deaf, that they would rather be deaf than blind; but the patient without a voice considers himself fortunate that he is neither blind nor deaf.

In advising the total removal of the larynx, one must appreciate the readjustments the patient must make and must evaluate his ability to make them.

His mental outlook should be given serious consideration. The patient who lives wholly within himself—the self-centered, brooding person who faces any crisis with the greatest difficulty—is poor material to make the mental readjustment necessary after total laryngectomy.

Although the larynx is described as the organ of speech, it is not necessary for speech. Useful audible speech may be obtained after removal of the larynx by use of the so-called "artificial larynx," as developed by the laboratories of the Bell Telephone Company, or by re-education and development of the so-called "esophageal voice."

The artificial larynx consists essentially of a flexible, noncorrosive metal reed that is placed in juxtaposition to a rubber membrane inside a brass sound box, a mouthpiece that fits into a metal stem at the top of the sound box and a flexible connection to the tracheal stoma. When this apparatus is being used for speaking, the air is inhaled through the hole in the side of the sound box and passes through the metal tube in its bottom, down through the rubber connecting tube and through the tracheal connection into the lungs. The air when exhaled tends to pass out by the way it entered, but if the hole in the side of the sound box is closed by the finger or thumb, the air is forced out around the reed. This causes the reed to vibrate and to produce sound, which passes out through the stem in the top of the sound box and to the rubber mouthpiece into the mouth, to be converted into speech. The artificial larynx is supplied to the patient early after the operation so as to offer a positive substitution for the lost power of speech.

The esophageal voice depends on the esophagus acting as an air chamber. The patient inflates his esophagus by swallowing air, creating a positive pressure that is thrown into air currents at the side of the tongue when its base is closed against the posterior pharyngeal wall. With exercise and training this action becomes automatic. (Dr. Schall then demonstrated 2 cases as examples of the successful use of these devices. In one, the patient had received a total laryngectomy, and by means of an artificial larynx was able to carry on successfully his work as a plumber. In the other, the patient was treated by external irradiation for an extensive carcinoma of both vocal cords. For three years he was free from disease. With recurrence and with the skin unable to stand further radiation, a total laryngectomy was performed. The patient developed an esophageal voice that permits him to continue his work as a fireman.)

CONCLUSIONS

In carcinoma of the larynx, as with cancer elsewhere, early diagnosis is of prime importance.

External irradiation is the ideal treatment, and it leaves a useful voice.

Laryngofissure, when indicated, gives a 75 to 82 per cent five-year cure.

Total laryngectomy, when necessary, does not always wreck the life of the patient, for this

result can be avoided by the use of an artificial larynx or of an esophageal voice.

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ERYTHROBLASTOSIS FOETALIS*

Report of a Case

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EVER since Diamond, Blackfan and Baty¹ in 1932 first designated as erythroblastosis foetalis, a syndrome characterized by the triad of hydrops, icterus gravis and anemia of the newborn, this interesting disease has been studied intensely. Darrow² in 1938 first suggested isoimmunization by the mother against fetal red cells as the basic etiology, but had no means of proving this theory. Levine and Stetson³ in 1939 were the first to point out that isoimmunization of the mother through the fetus can occur. Landsteiner and Wiener⁴ in 1940 discovered the occurrence of the Rh factor in 86 per cent of human beings as a dominant mendelian gene, and Levine with his co-workers^{5, 6} since 1941 have accumulated many data to prove that the Rh factor is at least one of the major etiologic causes of erythroblastosis foetalis. Javert^{7, 8} accepted the Rh factor as one of the causes, but suggested other necessary factors as further underlying conditions.

Most of the evidence, however, points to serologic phenomena, and erythroblastosis foetalis is most probably the outcome of an isoimmunization resulting from fetal antigens and subsequent hemolysis of the fetal red cells by maternal antibodies produced by these antigens, and transmitted from one circulation to the other in a process of diapedesis and dialysis.

Recently, a case of erythroblastosis foetalis of atypical form was observed in an infant who displayed icterus gravis as well as neonatal anemia, but no hydrops congenitum. A prompt diagnosis led to transfusions and resulted in cure and survival.

CASE REPORT

C. W., a 14-day-old boy, was admitted on October 14, 1942, with known intense jaundice of 5 days' duration. He was the second child of young, healthy parents, and was born at home without instrumentation. At birth he appeared normal and the attending obstetrician ob-

served no untoward symptoms or signs. The birth weight was not recorded, but the child appeared well developed. On the 9th postnatal day, a deep icterus became apparent and reached its maximal intensity 24 hours later. On admission the weight was 7 pounds, 2 ounces.

Both parents gave negative Wassermann and Kahn reactions. The mother was 19 years old and had a daughter of 21 months, born at term, who had at no time shown any degree of jaundice. She denied any miscarriages or stillbirths. The father was 24 years old and was jaundiced in infancy. Otherwise the family history was negative.

Physical examination was negative except for an intense icterus of the entire body. Enlargement of abdominal organs, and especially of the spleen and liver, could not be demonstrated by several examiners nor by a consultant, and roentgenograms of the long bones taken on October 16 gave no evidence of any pathologic lesions. The fragility test was negative, since hemolysis occurred in sodium chloride solutions ranging from 0.44 to 0.32 per cent, whereas in a normal control it occurred in solutions ranging from 0.40 to 0.30 per cent. A tentative diagnosis of erythroblastosis foetalis was made, substantiated by subsequent consultation and serologic studies by Dr. Philip Levine, of Newark, New Jersey. A total of three transfusions was given at intervals of about once a week. The essential features of the hemograms will be discussed in detail.

Serologically the father was Type A and the mother was Type O. The patient was also Type O, as was a sister of the mother. Agglutination of the patient's red cells by the mother's serum was positive, although both were Type O. This indicated the presence of some substances in the mother's serum that agglutinated the red cells of the infant. These substances were later proved to be anti-Rh agglutinins.

The initial hemogram of the patient gave a count of 1,520,000 erythrocytes. The white-cell count was 42,000, with 39 per cent mature and 6 per cent immature polymorphonuclear leukocytes and 5 per cent myelocytes, as well as 4 per cent nucleated red cells. The hemoglobin was 32 per cent (Sahli), and the color index 1.06. Marked anisocytosis and polychromasia were present in this as well as in all subsequent stained smears except the last. During the next 2 days the red-cell count fell to 1,500,000, and the white-cell count to 34,000, with 30 per cent polymorphonuclear leukocytes and 18 per cent myelocytes; the nucleated erythrocytes increased to 7 per cent.

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On October 17, a transfusion of 50 cc. of whole blood from a professional donor of Type O was given without regard to the Rh factor. The red-cell count reached a maximum of 2,290,000; the white-cell count decreased to 12,300, with a minimum of 19 per cent polymorphonuclear leukocytes, and an additional 8 per cent immature and 8 per cent myelocytic granulocytes. The hemoglobin rose to 46 per cent, with a color index of 1.04. Simultaneously with the first transfusion, 1 mg. of vitamin K and 0.3 cc. of liver extract were given daily, and the patient showed a normal weight-increase curve.

On October 23 the red-cell count had fallen to 2,090,000. The white-cell count was 18,500, with 24 per cent mature and 5 per cent immature polymorphonuclear leukocytes and 9 per cent myelocytic granulocytes, and 6 per cent nucleated red cells. The hemoglobin was 39 per cent, with a color index of 0.89. A second transfusion of 50 cc. of whole blood was therefore given from the original donor, after routine cross matching at room temperature. This transfusion was followed by fever and facial twitchings of the recipient. The red cell count reached 3,000,000 the day after the transfusion. The white-cell count fell to 11,600 after a slight increase during the period of reaction. The polymorphonuclear leukocytes increased to 33 per cent, the immature granulocytes remained stable at 5 per cent, and the myelocytes decreased to 5 per cent. The nucleated erythrocytes reached a maximum, 16 per cent, on the day following the transfusion, decreasing to zero 5 days later. The hemoglobin increased to 62 per cent, whereas the color index remained stable at 1.03. Physical examination revealed that the icterus had greatly decreased and that the weight had increased in a regular curve.

On November 2, a third transfusion of 50 cc. of whole blood was deemed necessary to hasten complete recovery. A new donor was found in the mother's sister, whose cells were compatible by Levine's⁹ modified cross-matching technic.* Following this transfusion the red-cell count rose rapidly to 3,000,000, at which level it stabilized, with complete disappearance of the nucleated erythrocytes. The white-cell count rose from 13,900 to 28,000 owing to a minor skin infection, but decreased in a few days to 17,000. The polymorphonuclear leukocytes increased steadily from 30 to 55 per cent, the immature as well as the myelocytic granulocytes disappeared, and the hemoglobin reached 60 per cent, with an average color index of 1.0. The icterus disappeared completely, and by November 21, when the patient was discharged, the weight had reached 8 pounds, 8 ounces. The anisocytosis and polychromasia had disappeared.

Blood samples of the mother were submitted to Dr. Levine, who gave the following report:

The mother's blood is in Group O; it is Rh-negative with each of the three varieties of anti-Rh serums, and positive with anti-Hr serum. The serum contains anti-Rh agglutinins with a titer of about 1:50 and its specificity corresponds to that of an anti-Rh₁; that is, it gives 85 per cent reactions.

Subsequent physical examination and hemograms of the patient were negative. He was last seen on January 26, 1943, or 2 months after discharge, at the age of 4 months. He appeared physically well and displayed no signs of jaundice or other residual, and was considered cured. The red-cell count was 4,290,000 and the white-

cell count was 13,000, with 34 per cent polymorphonuclear leukocytes plus 2 per cent immature granulocytes. The hemoglobin had risen to 78 per cent, with a color index of 0.90. Neither anisocytosis nor polychromasia was evident. It should be pointed out that the severe icterus and the facial twitchings during the course of the disease may very well have been associated with kernicterus, and that, therefore, cerebral palsies and retardation in physical and intellectual development must be watched for during the next 6 months to be certain that this damage did not occur.

DISCUSSION

The importance and role of the Rh factor in the pathogenesis of erythroblastosis foetalis and its logical therapy were well pointed out by Levine and his co-workers^{5,6} in 1941-1942. The existence of qualitative differences in the Rh agglutinogens in human Rh+ blood was first demonstrated by Wiener¹⁰ in 1941. Levine⁹ in 1941 claimed that about 90 per cent of intragroup transfusion reactions are due to isoimmunization, either because of repeated transfusions or because of diapedesis of fetal blood in Rh- women, although anti-Rh agglutinins cannot always be demonstrated. He assumed that the anti-Rh antibody is fixed to the tissue cells of the reticuloendothelial system. To prevent such accidents all Rh- recipients should be transfused with Rh- blood only. In cross matching, the patient's serum and donor's cells should be incubated at 37°C. for the fifteen to thirty minutes before the result is reported, since anti-Rh agglutinins frequently behave like warm agglutinins, as in the present case. However, even this modified cross-matching technic is reliable in less than half of the cases, and should not take the place of typing for the Rh factor in well-organized hospitals and medical centers. Levine's⁹ article should be consulted for details of the modified cross-matching technic.

The clinical triad of erythroblastosis foetalis consists of fetal hydrops, icterus gravis neonatorum and neonatal anemia. This patient presented a deep icterus as well as neonatal anemia with excessive normoblasts and progressive decrease of the peripheral red-cell count. However, the fact that hemolysis became grossly evident as late as nine days after birth does not argue against the isoimmunization theory of erythroblastosis foetalis, since several authors have made such reports. The suggestion has been advanced that the delayed reaction—that is, hemolysis—may be produced in breast-fed infants by the ingestion of colostrum. This, however, does not pertain to our observation, since the patient was bottle fed. Another theory holds that the agglutinins of the mother can be stored in the fetal tissues or remain in combination with other red cells, to be released

*The tubes are incubated at 37°C. for thirty minutes, then centrifuged at 500 r.p.m. for one minute; they are then inspected for agglutination, both grossly and under the microscope.

later, although it is not as yet clear what mechanism brings about this release. Yet this last theory may be applied to the present case, in which after transfusion with nonagglutinating blood jaundice apparently became clearly visible nine days after delivery, and in which isoagglutinins were demonstrated in the mother's blood. Furthermore, (third transfusion) higher hemoglobin levels and red-cell counts were maintained.

The theory of Levine and his co-workers is in essence that 87 per cent of all human beings are Rh+ and 13 per cent are Rh-. Levine et al.^{5,6} also found that 90 per cent of mothers whose infants developed erythroblastosis foetalis were Rh-, and all these women were married to Rh+ husbands. If an Rh- woman bears a child by an Rh+ man, all offspring will be Rh+ if the husband is homozygous, but only half if he is heterozygous (mendelian dominant), and only these may develop erythroblastosis. This occurs oftener in the second Rh+ child (as in our case) and in subsequent children, since isoimmunization is said to be initiated by the first pregnancy. During this period of isoimmunization the Rh+ red cells from the fetus apparently pass through the placental membranes into the Rh- maternal circulation, where they stimulate the production of antibodies. These antibodies then pass back into the fetal circulation, and if they there attain a suitable concentration produce agglutination and, secondarily, hemolysis of the fetal red corpuscles, the equivalent of the agglutination effect in vitro.

At birth the fetal and maternal circulations are permanently severed and the exchange of Rh+ cells between fetus and mother and of anti-Rh antibodies between mother and fetus ceases. Yet fetal hemolysis will continue until all anti-Rh antibodies are neutralized—that is, used up. This occurs normally in eight to fourteen days post natus unless the hemolysis is so severe as to bring about fetal death. At autopsy, even the brain nuclei may show deep jaundice (kernicterus), a characteristic peculiar to 25 per cent of cases in which death is due to erythroblastosis foetalis. To combat this hemolysis in the infant, frequent transfusions of Rh- cells are required, since these cells cannot be hemolyzed by the anti-Rh antibodies, and thus sufficient erythrocytes are left to maintain vital functions. The infant will, however, counteract this hemolysis also by increased red-cell production. The result of this increased hemopoiesis is the appearance of many nucleated erythrocytes in the peripheral blood stream, another characteristic of this neonatal anemia.

Javert⁸ gave the incidence of erythroblastosis foetalis of all types as 0.23 per cent, and its cause of fetal death as 3.2 per cent. The nearer to term

the disease develops the better is the prognosis. It occurs more frequently in multiparas than in primiparas since preceding pregnancies predispose to it. Javert concurs to a large extent with the theory of Levine, but finds sufficient exceptions to maintain that the Rh factor cannot be the sole cause of erythroblastosis foetalis, since other agglutinogens may also produce isoimmunization of the mother.

SUMMARY AND CONCLUSIONS

A case of erythroblastosis foetalis with icterus gravis and neonatal anemia in a nine-day-old infant is reported, and the recent pertinent literature and theories are briefly reviewed.

Serologic studies substantiated the fact that the Rh factor was at least one of the major etiologic causes in the pathogenesis. However, it seems that other fetal antigens may also stimulate the production of maternal antibodies that bring about fetal hemolysis as late as nine days post partum. The true mechanism of development is still obscure, but it seems that the antibodies can be stored, or may at least remain latent, in the fetal red blood cells or tissues even after separation of the two circulations, and can be liberated by still unknown processes. Ingestion of colostrum did not produce their liberation in the present case.

Therapeutically, repeated transfusions of properly selected and cross-matched blood, preferably by anti-Rh serum, or by Levine's modified technic, are the only successful methods. It should be stressed that Rh- blood is important for the infant with erythroblastosis foetalis for at least the first week after birth. This need becomes less and less important as evidence of hemolysis diminishes in the second and third weeks of life.

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HISTAMINE BY MOUTH IN THE TREATMENT OF VASOMOTOR RHINITIS*

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SINCE the work of Dale and Laidlaw¹ on the role of histamine in anaphylaxis and allergy was published in 1919, many papers on this subject have been written. Ramirez and St. George² in 1924 first attempted the use of histamine as a therapeutic agent, but with inconclusive results. Stahl and Masson³ applied histamine to skin scarifications and had encouraging success, although the technic of dosage was crude. Dzsinich⁴ emphasized the importance of extremely small doses and worked out an effective scheme of treatment. Alexander and Elliott⁵ had excellent results in urticaria with intravenous injections of large doses. Attention should also be paid to the papers by Farmer,⁶⁻⁸ who reports a great number of cases treated with Dzsinich's technic and gives a complete review of the work done in this field.

Although most of the investigators have tried to imitate the technic used in specific desensitization, and to build up a so-called "specific non-specific" resistance to histamine by giving frequent and steadily increasing doses, a few—mostly accidental—observations have shown that histamine has an immediate beneficial effect in the allergic manifestation. Thus far only Stahl and Masson have tried to use this effect in therapy. They applied histamine by skin scarifications during an attack of asthma and observed a beneficial effect.

Since the effect of histamine is almost immediate and is transient, it is evident that the drug should be given at frequent intervals. For the average patient, injection, whether given by the intradermal, subcutaneous or intravenous route, is impractical, and we have been led to investigate further the effectiveness of giving histamine by mouth.

Although it is generally considered that histamine is largely destroyed by the gastric juices, there are a few reports in the earlier literature indicating that small amounts may be absorbed through the intestinal wall (Meakins and Harington,⁹ Ivy and McIlvain¹⁰ and Koessler and Hanke¹¹).

That histamine given by mouth is absorbed promptly and has a definite action is shown by the variety of toxic effects. For example, one of

our patients developed a characteristic flushing of the face within ten minutes after taking 13 drops of a 1:1000 dilution of histamine, and all treatment with histamine had to be discontinued because of severe menstrual pain. In another case, severe headaches occurred regularly within ten minutes after each dose of histamine, but they subsided in another ten minutes. Three patients developed abdominal cramps and pain following the taking of histamine. One of them had taken the drops shortly after a highball, and it is likely that the permeability of the stomach wall was altered by the alcohol. One of us (R. J. S.) has had abdominal cramps repeatedly following experimental doses of histamine.

Even more suggestive are specific reactions in which the original symptoms are duplicated. Thus, when histamine is given in doses larger than the empirically established optimum, patients with vasomotor rhinitis may have increased nasal obstruction or rhinorrhea, and those with asthma develop a wheeze.

It is apparent that histamine is absorbed from the gastrointestinal tract and that the same physiologic reactions are obtained as with parenteral injection.

The technic for its administration by mouth requires close attention to details. The therapeutically effective dose varies greatly among patients, but for each it remains quite constant over a long period of time. Our method is to start with a 1:1000 dilution and a dose of 1 drop in a glass of water. The patient is asked to observe the reaction closely. He finds that too large a dose aggravates his symptoms and too small a dose causes no change, but that the correct dose relieves him within fifteen or twenty minutes. If there are no bad effects, he is advised to increase the dose by adding 1 drop each day until toxic effects appear. Thereafter he is maintained on the dose that is just below the toxic level, and this dose is repeated as often as is necessary to control the symptoms.

The dose may vary from 1 drop of a 1:1000 dilution to 25 drops of a 1:100 dilution, but the average dose is 5 to 7 drops of the 1:1000 dilution. The necessity for perseverance and for intelligent cooperation by the patient is obvious. In most of our patients, oral histamine therapy was given only

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TABLE 1.

CASE No.	HOSPITAL No.	SEX	AGE		FAMILIAL HISTORY OF ALLERGY	POSITIVE SKIN TESTS
			yr.	yr.		
1*	374067	M	23		+	Pollen
2	371450	M	12		-	None
3	209434	F	39	34		Pollen, dust, wheat and feathers
4	354350	M	64	22	-	Wheat
5	121308	F	49	44		Animal hair, dust, kapok, orris, wheat and Alternaria
6	148644	F	22	10		Pollen
7	367109	F	22	15	-	None
8	369445	F	40	39	-	None
9	24672	F	21	16		Feathers
10	325777	F	23	22	-	Kapok, orris, dog hair, dust and ragweed
11	313471	M	54	54	-	Feathers
12	372486	F	18	16		None
13	264193	F	42	25	-	Kapok, orris, pyrethrum and cat hair
14*	203782	F	41	41	+	Ragweed
15	377093	F	27	19	+	None
16	187845	F	28	26	-	None
17	365560	F	45	35	-	Many, including pollen
18	160532	M	48	44		None
19	366737	F	14	14	-	None
20	331470	F	42	34		Ragweed, kapok, goose feathers, orris, Alternaria, dust and cat hair
21	10257	F	41	34		None
22	357832	F	21	21		None
23	298733	F	42	40	+	Orris, house dust and pyrethrum
24	41826	M	12	11	+	None
25	366441	F	24	19	+	None
26	171475	M	58	45	+	None
27	356021	F	31	31	-	None
28	107864	F	79	74	+	None
29	306894	F	35	23	-	Cherry
30	307068	F	15	14		House dust, kapok and wheat
31	378117	F	35	35		Ragweed, house dust, feathers, egg white and dog hair
32	178422	F	35	32	-	Orris and wheat
33	102205	F	32	27	-	Feathers

CASE No.	PREVIOUS TREATMENT		OPTIMUM DOSAGE OF HISTAMINE	RESULT	REMARKS
	KIND	RESULT			
1	None		7 (1:1000)	None	Patient unco-operative
2	None		1-5 (1:1000)	Excellent	Effect immediate
3	Vaccines	None	12 (1:1000)	Excellent	
4	Wheat injections	None	15 (1:1000)	Complete relief	
5	Vaccines and elimination	Slight improvement	6 (1:1000)	Excellent	
6	Pollen injections	Slight improvement	23 (1:1000)	None	Patient unco-operative
7	Vaccines	None	5-7 (1:1000)	Good	
8	None		1-2 (1:1000)	Good	
9	Vaccines	None	5-6 (1:1000)	Excellent	Abdominal cramps
10	Vaccines and elimination	None	2 (1:1000)	Fair	
11	Vaccines and elimination	None	10 (1:1000)	Excellent	
12	None		1 (1:1000)	Excellent	
13	Vaccine and nasal therapy	None	5-15 (1:1000)	Fair	Effect diminished in spite of larger doses
14	None		2-3 (1:1000)	Excellent	
15	Ephedrine packs	None	3-4 (1:1000)	Complete relief	Nasal mucosa became normal
16	Vaccines and elimination of dust	None	7 (1:200)	Good	Results affected by menstruation
17	Ragweed injections	None	4 (1:1000)	Complete relief	
18	Vaccines and nasal therapy	Moderate improvement	8-13 (1:1000)	Slight or none	Patient unco-operative
19	None		15 (1:1000)	Excellent	
20	Vaccines and elimination	None	7 (1:1000)	Excellent	
21	Vaccines and nasal therapy	None	12 (1:1000)	Good	
22	None		6 (1:1000)	Excellent	
23	Dust injections and nasal therapy	None	3 (1:1000)	Excellent	Abdominal pain
24	Vaccines	None	15 (1:100)	None	Symptom free at seashore
25	None		3-4 (1:1000)	Excellent	
26	Vaccines	None	6-12 (1:100)	Good	
27	Vaccines	None	6 (1:1000)	Excellent	
28	Vaccines	None	2 (1:1000)	Excellent	
29	Dust injections and elimination	Slight improvement	5-15 (1:1000)	Fair	Large doses required during menstruation
30	Vaccines and elimination	Slight improvement	11 (1:1000)	Excellent	
31	Elimination	None	17 (1:200)	Excellent	
32	Vaccines and orris injections	Slight improvement	11 (1:200)	Excellent	Beneficial effect eventually lost
33	None		16 (1:100)	None	

*Case of hay fever; all others, vasomotor rhinitis.

after treatment with other methods had been followed, often for years, without success.

Two of us (J. C. G. and R. J. S.) have made routine use of histamine in treating a large group of private patients suffering from vasomotor rhinitis during the last four years. We are convinced of its value as an agent for symptomatic relief. Unfortunately, however, the private cases cannot be included in a statistical report because other therapeutic procedures—vaccines, thyroid and diets—were used at the same time with the histamine.

To test the value of histamine alone, a small group of clinic patients was selected, and, as a rule, no changes in their routine way of life were made except to prescribe histamine in doses as described above. Forty cases of perennial vasomotor rhinitis and 6 of seasonal hay fever were chosen. Of this group 13 were lost and the end results are unknown. The balance (33 cases) are listed in Table 1. In 3 cases, treatment had to be discontinued because of the lack of co-operation by the patient. Of the remaining 30 cases, 1 (Case 24) showed no effect up to a dose of 15 drops of 1:100 dilution, and in another (Case 33) there was temporary relief from 5 drops of 1:1000 dilution, but the patient later became refractory and doses up to 16 drops of 1:100 dilution were ineffective. In the other 28 cases, histamine produced repeatedly or regularly an immediate beneficial effect on the nasal symptoms, and most of these patients have been followed over a period of several months. This series is being rapidly extended, and histamine is being tried in other conditions with results that will be reported later.

The most striking therapeutic effects so far observed have been seen in the cases of vasomotor rhinitis. In such cases, within ten to twenty minutes after a dose of histamine by mouth the symptoms cleared and nasal obstruction, sneezing and watery discharge ceased. The benefit is more marked than that derived from ordinary nasal sprays or drops, and it usually lasts for several hours. In rare cases the symptoms return in less than an hour, but in others the relief from a single dose lasts for a full day or more. When the symptoms recur, another dose is taken, with the same effects. This immediate symptomatic relief is the main objective of our technic, and it should be noted that the effect of single doses is prolonged as time goes on—that is, histamine is needed less and less frequently. Patients who in the beginning needed six or eight doses of histamine daily, after a few weeks of treatment needed only two or three doses daily, and later on only occasional doses once every few days.

The following case reports illustrate the method and the results:

CASE REPORTS

CASE 17. This 45-year-old, married woman had had a stuffy nose persistently since the age of 35. She had also had migraine. Skin tests were positive for a large number of allergens, among them ragweed. Ragweed injections were given weekly or biweekly from July 31 to September 8, 1942, without improvement. During October, the patient's condition became somewhat better, but nasal obstruction persisted. On October 19, histamine treatment was started. On November 9, the patient reported on her 3 weeks' experience: doses up to 3 drops of 1:1000 dilution had been ineffective, but 4 drops brought complete relief within 20 minutes. In November, she was taking 4 drops once a day before bedtime and was sleeping the whole night.

CASE 25. This 24-year-old, married woman had had perennial vasomotor rhinitis and headaches since the age of 19. She had had attacks of urticaria for years, and had suffered from cold hands and feet as long as she could remember. Her father had had hay fever. Her nose had been packed with ephedrine but without any permanent effect. On September 28, 1942, the nasal mucous membranes were pale and boggy. Skin tests were negative. Therapy with histamine in 1:1000 dilution by mouth was begun on October 5. On October 13, 3 to 4 drops of this dilution relieved the headaches and the nasal obstruction within 15 to 20 minutes. On November 2, the headaches and nasal obstruction had developed only once during the last 3 weeks and were promptly relieved by 4 drops of histamine. On November 6, examination of the nose showed normal mucous membranes. Meantime, however, the urticaria remained unimproved and the patient had daily eruptions. A new oral course of histamine was started.

CASE 9. This 21-year-old woman had had perennial vasomotor rhinitis since the age of 16. Intradermal tests had been positive for goose feathers, but elimination of feathers and dust as well as treatment with vaccines had been of no benefit. On August 4, 1942, oral doses of histamine in 1:1000 dilution and of thyroxin were begun. On August 18, the patient was still sneezing but 6 drops of histamine always brought relief. The dose caused stomach cramps, however, and the treatment had to be discontinued. Through the fall histamine was tried off and on, but always with the same effect. A dose of 6 drops brought relief from nasal symptoms, but they caused stomach cramps. When the drops were taken before meals instead of after them, 4 drops was ineffective, but 5 drops gave complete relief and the stomach pain was much less severe.

CASE 4. This 64-year-old baker had had chronic vasomotor rhinitis since the age of 22, becoming worse recently. Nasal discharge and sneezing made it difficult for him to work. During a vacation in Florida in the winter of 1941-1942 he was entirely free from symptoms, but on the first day of work on his return, sneezing and nasal discharge began again in full strength. From May 25 to October 2, 1942, injections of wheat extract were given each week, but with hardly any improvement. On October 2, a vaccine injection was given and oral histamine therapy, combined with thyroxin in doses of 30 mg. twice a day, was begun. On October 23, doses of histamine up to 14 drops of 1:1000 dilution had been ineffective, but 15 drops gave regularly almost complete relief. If this dose was taken every morning before going

to work the nose cleared within 15 to 20 minutes and remained clear during the time at work. Only this single dose was needed each day. On November 20, the patient was still well.

CASE 28. This 79-year-old, married woman had had a stuffy nose since the age of 74. Treatment with vaccines had been of no benefit. On October 1, 1942, she was miserable with continuous nasal discharge and sneezing and was unable to sleep. Histamine by mouth was begun. On October 22, she took up to 6 drops of 1:1000 dilution. Relief came from 1 or 2 drops, but she misunderstood the directions and increased the quantities. As a result, her nose ran more than ever. As soon as the dose was reduced to 2 drops, however, relief was obtained. On November 23, the patient was taking this small dose four or five times a day and felt better than she had for 4 years.

SUMMARY AND CONCLUSIONS

The occurrence of good results in all except 2 of 30 cases is more than a coincidence. That histamine is absorbed from the gastrointestinal tract is demonstrated by Farmer's results in guinea pigs and by the occurrence of toxic reaction as reported above. The object has not been to build up a general resistance to histamine but rather to control the symptoms by repeated small doses. The wide variation in patients' susceptibility to histamine is very interesting and constitutes the chief difficulty, if not the actual danger, in treatment of this sort. In the present series, once the proper dose was determined, other doses of this same size repeated their physiologic effect from time to time indefinitely. It has also been observed that the good effect of single doses seems to last longer as the treatment is continued for weeks or months.

This observation somewhat contradicts the current attempts to explain the effect of histamine in allergic diseases on the basis of mithridatization or a desensitization against histamine.

Histamine is sometimes less effective during menstruation or a few days before it. This is understandable in view of the fact that allergic manifes-

tations are frequently more severe at this time. The effectiveness of histamine and therefore the size of the dose depend also on the functional state of the stomach. The amount of histamine that passes undestroyed through the wall of an empty stomach is quite different from that which is absorbed at the height of gastric activity. Because the dosage of histamine is so delicate and the variations in absorption so great, it is imperative to maintain basic conditions rigorously. It seems advisable to take histamine only before meals, when the stomach is empty.

Sometimes unpleasant by-effects cannot be avoided. If severe stomach cramps appear at the level that gives therapeutic results, or if menstruation is strongly affected, it may become necessary to discontinue the treatment as was the case in 3 of this series.

Oral histamine therapy is not a panacea. Much work remains to be done on the problem, but so far it can at least be said that it brings results that are definitely superior to those obtained by the other methods of treatment of vasomotor rhinitis, which are so cumbersome and unsatisfactory.

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MEDICAL PROGRESS

THE DIAGNOSIS OF GOUT*

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THE diagnosis of gout is frequently not made because the patient does not exhibit the classic features of chronic gout. This common diagnostic error and the ensuing therapeutic mistakes will continue to occur unless physicians become increasingly alert to the various manifestations of the disease. It is hoped that this treatise, dealing solely with those features pertaining to diagnosis, will help serve the above purpose.

Gout is a hereditary constitutional disease, preeminently of males, occurring at any age and in most cases characterized by recurring attacks of acute arthritis. The clinical picture may, however, vary from an asymptomatic hyperuricemia to a severe, crippling joint disease even in the same patient. The articular inflammation of both acute and chronic gouty arthritis is caused by deposits of sodium urate (tophi), which may also be found in many other tissues. Although the exact etiology of the disease remains unknown, it is rightly classed as one of inborn metabolism, the fundamental metabolic defect, the inability of the organism to dispose of uric acid, being evidenced by a hyperuricemia. The latter may be present long before the ailment assumes its striking articular form. Space does not permit a discussion of the various theories advanced to explain the altered excretion of urates, the hyperuricemia and the formation of urate deposits in the tissues. It is sufficient to state that these phenomena remain three of the enigmas of the disease.

PATHOLOGY

Only those pathological features of the disease that pertain to a better diagnostic understanding will be discussed. The changes observed are dependent on the deposition of sodium urate in the various tissues and the inflammatory and degenerative changes resulting therefrom. The urate deposits surrounded by tissue exhibiting inflammatory and foreign-body reactions constitute the one

pathognomonic lesion of the disease, and are readily demonstrated provided the tissues to be examined are properly fixed and stained.¹ Many of the anatomic alterations observed in the late stages of gout are the result of the ill-understood arterial and arteriolar sclerosis that frequently manifests itself as the disease advances.

Deposits of urate in articular structures are the cause of the most frequent disability resulting from gout. No joint is exempt, although certain ones are more frequently involved than others,²⁻⁴ for example, the joints of the lower extremities as compared to those of the arms. The metatarsophalangeal joints of the great toes are most regularly affected and may be the only site. The small joints affected in order of frequency are those of the feet, the ankles and the wrists. The knees, elbows, shoulders and hips are less commonly involved. The sacroiliac and sternoclavicular joints and the articulations of the spine, jaw and larynx most rarely contain foci of urate deposition.

The term "tophus" has through general usage come to denote a urate deposit in tissues other than joints. These abarticular tophi are most commonly seen in the helix or antihelix of the ear, the olecranon and prepatellar bursae and the tendons of the fingers and wrists, toes, ankles and heels. Less frequently they are met with in the skin of the palms and soles, the tarsal plates of the eyes, the nasal cartilages, the fingertips, the tendinous expansion of the muscles and the cornea and sclerotic coat of the eye.⁵ The kidneys may also be the seat of urate precipitates. Very rarely they have been found in the corpus cavernosum, the prepuce of the penis, the aorta, the myocardium and aortic valves, the tongue,⁶ epiglottis and vocal cords, and the arytenoid cartilages. Occasionally the crystals have been recovered from the sputum of gouty subjects.⁷ The isolated reports of urates in the central nervous system and its coverings have never been verified. Such abarticular deposits are followed by the foreign-body inflammatory reaction previously referred to, and vary in extent and degree with the vascularity of the affected tissue.

The renal lesions observed in gout have been called *gouty nephritis*, *gouty form of Bright's disease*, *interstitial or arteriosclerotic nephritis* and *renal impairment of gout*. This varied terminology indicates that no unanimity of opinion has

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existed concerning the nature of these changes, but all writers are agreed that the incidence of kidney disease is higher in gout than in other chronic disorders, such as rheumatoid arthritis, diabetes mellitus and pernicious anemia. Few if any, however, argue that anatomic alterations of the kidney can be demonstrated as the primary cause of gout.

The incidence of arteriosclerosis and hypertension is higher in gouty subjects than in a control group of comparable age.⁸⁻¹¹ The latter is usually a late manifestation. The triad of arteriosclerosis, nephrosclerosis and increased arterial tension frequently leads to hypertrophy of the left ventricle. Marked arteriosclerotic degeneration of the aorta is not uncommon. Extensive coronary and cerebral vascular disease may be the immediate cause of death. Other pathologic changes associated with the disease are similar in nature and extent to those found in any corresponding age group.

GENERAL CONSIDERATIONS

Incidence

The incidence of gout is unknown. Undoubtedly, many more cases are seen in private practice than in hospitals because acute gouty arthritis is, as a rule, self limited and of short duration. Hench¹² estimates that 5 per cent of all patients with joint disease seen at the Mayo Clinic have gout. This is a much higher incidence than has been found in most other clinics. The evidence derived from pathological studies reveals an incidence varying from 1 to 5 per cent.^{13, 14} Despite such marked discrepancies, gout does not appear to be a rare or declining disease. As stated previously, the diagnosis frequently is not made because the patient fails to exhibit the classic features of chronic gout.

Heredity

The earliest medical writers have stressed the hereditary nature of gout. A familial incidence as high as 75 per cent has been observed.^{2, 15, 16} The propensity of the disease to pass over one generation is a hindrance to the investigator gathering genealogic data. It is commonly stated that women, although infrequent victims of gout, are likely to transmit it to their children.⁷ Thus, a patient may inherit his maternal grandfather's gout although his mother never experienced any clinical manifestations of the disease.

Sex

Slightly over 95 per cent of all patients affected with the disease are males. The explanation for this striking difference in the incidence of gout in the two sexes is unknown.

Age

Gout is an inherited disease. Its potentialities are assumed to be present at birth. The finding of hyperuricemia in apparently normal young relatives of gouty patients and its presence with or without tophi in adults for years prior to the onset of articular complaints indicate that the disease antedates the appearance of symptoms. It rarely manifests itself in infancy or adolescence. Acute arthritis occurs with increasing frequency in the second to the sixth decade, being commonest in the forties. The first evidence of the disease, however, may not appear until late in life. Cases are on record demonstrating the initiation of symptoms in the sixties, seventies and eighties. In such cases the attacks as well as the subsequent course tend to be mild. The converse is likewise true: onset at an early age frequently portends severe seizures, often polyarticular in distribution, and may lead to extensive crippling and severe vascular nephritis before middle life.

Race and Climate

There is at present no accurate information concerning the relevance to gout of either race or climate.

Habits and Occupation

Those who believe that gout is the nemesis of high living cite a higher incidence among people whose occupations are conducive to overindulgence in food and drink. Until more conclusive statistical information concerning the occupational incidence of the disease is available, it is impossible to evaluate past statements or to make further comment.

Clinical Manifestations and Course

The symptomatic or articular manifestations of gout are designated by various terms. The acute attacks, which are followed by complete remissions, have been called "acute gout" and "regular" or "acute recurrent gouty arthritis," in distinction from chronic gout, signifying chronic gouty arthritis with or without tophi. Because the disease runs an extremely diversified and irregular clinical course, the simple yet satisfactory classification of acute and chronic gouty arthritis has been generally adopted.

The onset of the first attack of acute gouty arthritis is as a rule dramatic. The patient, usually a healthy-appearing middle-aged man, is suddenly seized with severe, sometimes excruciating, pain, often in one of the metatarsophalangeal joints. Although such attacks frequently begin at night, they may occur at any time. Within a few hours of the onset, the afflicted joint becomes swollen, red, hot and exquisitely tender. The swelling may

appear so rapidly that within a few hours the patient is unable to remove his shoe without cutting it. The inflammatory edema is much more marked than in other acute arthritides and often extends some distance beyond the joint margins. Effusion into the large joints is not uncommon. At the peak of the attack the intense swelling of the foot, accompanied by redness and extreme heat, resembles septic inflammation or an extensive cellulitis. There may be an associated lymphangitis. The skin is red, tense and shiny. The superficial veins are distended. The pain, often described as crushing and usually worst at night, generally confines the patient to his bed or room because weight bearing is intolerable.

As tenderness and redness subside, pitting edema is demonstrable. With the disappearance of the swelling, the overlying skin become loose and thin and desquamation of the cutis and itching may follow. The combination of these findings is rarely encountered in other types of acute arthritis, and is therefore of singular diagnostic significance. The attack subsides spontaneously within ten days to a few weeks, with complete restoration of normal joint function.

Approximately 50 per cent of the initial attacks are confined to the first metatarsophalangeal joint, but not infrequently other joints are affected at the same time. The neighboring metatarsal and tarsal joints or those of the opposite foot may be involved simultaneously or in rapid succession. A bursa, more commonly over the olecranon or patella, may be the site of an attack. The younger the patient, the more likely is the attack to be polyarticular and migratory in nature. Fever, again more prominent in young patients, is usually mild, rarely lasts more than a few days, and may be absent. The severity of the initial attack varies greatly. In some cases the acute illness is extremely mild and lasts only a few days. Occasionally one sees abortive attacks.

Physical examination at the time of the initial attack of gouty arthritis is usually negative except for the articular findings. Maximal joint tenderness is usually present on the medial aspects of the involved joint. A tophus, unknown to the patient, may be found in the helix of the ear, indicating that the disease has been present for some time. The clinical course subsequent to the initial attack, although usually conforming to a distinct pattern, may vary considerably. Very rarely the patient remains symptom free altogether, or for an interval of many years, as exemplified by a case in which the initial seizure at twenty-seven years of age was succeeded by a second one sixty-two years later. In the benign form two to six distinct attacks may be scattered over a period of

thirty to fifty years or concentrated in one of the middle decades of life.

The recurrent attacks of acute arthritis are commonly followed by remissions during which the patient experiences no articular symptoms whatever. These latent periods tend to become progressively shorter until acute episodes occur once or twice yearly, often with a certain regularity. Some patients, for unexplained reasons, are taken ill each spring and fall. At this stage of the disease, the patient is less likely to experience complete remissions and his illness is approaching or has entered on the phase of chronic gouty arthritis or chronic gout. In a few cases, most of which belong to the juvenile form, the disease is chronic from the outset. More frequently, a period of five to forty years separates the initial attack from the chronic phase.

In the advanced stages of the disease, an increasing number of joints are affected, particularly those of the feet, ankles and wrists and the knees and elbows. Subcutaneous tophi, representing infiltrations of urates into periarticular and bursal tissues, are frequently found and are responsible for the knobby deformities of the knuckles and interphalangeal joints. They may also be seen about the knee and elbow and along the tendons of the fingers, toes, ankles and wrists. Tophaceous deposits occur in nonarticular cartilage; indeed, their commonest site in chronic gout is the helix of the ear. They vary in size from a barely palpable nodule to deposits measuring as much as 5 cm. in diameter. Their presence in cartilage may be unattended by any symptoms, but in subcutaneous tissue visible inflammatory reaction usually results. There the deposits appear first as slightly red elevations that gradually develop into white, cream-colored or yellow nodules of varying size. The skin overlying a tophus may ulcerate and discharge a white, chalky material that on microscopic examination shows the characteristic acicular crystals of sodium urate. Such ulcerating lesions may occur anywhere on the body surface but are commonest on the hands and feet. They rarely become infected.

Tophi are found in about 50 per cent of all cases of gout. In some cases they antedate the acute joint disease, whereas in others they are not found until ten to thirty years after the initial attack. They should not be confused with the subcutaneous nodules of rheumatic fever and rheumatoid arthritis. Because they constitute the one pathognomonic lesion of gout, they should always be searched for. Regardless of whether or not a nodule has the characteristic clinical appearance of a tophus, it is unwise to accept it as such until it has been needled and the monosodium urate crys-

tals have been demonstrated or a positive murexide reaction has been obtained.

The term "irregular gout," still used by some writers, originally designated a group of nondescript symptoms that in the past has also been referred to as lithemia or as a uric acid, lithic acid, or gouty diathesis. The clinical markings of irregular gout were most varied and apparently incorporated all the inexplicable complaints that occurred in the gouty subject. Some of these were probably results of medication with impure preparations of colchicum. The term was, however, also applied to the indefinite ailment of members of gouty families who had never suffered an acute attack of gouty arthritis. In these cases the symptoms were often ascribed to an excess of uric acid proved by the finding of urate sediment in the urine! Neither this type nor an irregular type of articular gout postulated by some current writers^{17, 18} deserves recognition. The patients described, usually women, exhibit none of the characteristic findings of symptomatic gout. Their arthritis is insidious in its onset and slowly progressive, without remissions or associated tophi. As a rule, these patients are advanced in years and show only a slightly higher than normal blood uric acid. In a few cases, hyperuricemia, probably due to nephritis, and rarely a family history of gout are found. If such variations of gout occur, they should be susceptible to pathological proof, and when present generally show favorable response to the therapy administered for acute gouty arthritis. The propriety of using such terms as "visceral" or "abarticular gouty" is equally dubious.

PREMONITORY SYMPTOMS

The specific changes that presumably take place in the gouty subject between birth and the onset of the clinical illness have not been studied, but hyperuricemia has been demonstrated at an early age.^{16, 19, 20} Whether it is ever present at birth is unknown, nor are bodily alterations immediately preceding the gouty seizure, the so-called "larval state," understood. Many patients experienced no premonition of the impending attack; some even feel their best at that time. Others complain of anorexia, nausea, indigestion, melancholia, stiffness, aching, polyuria and nocturia. The diuresis may be taken as an expression of the altered mineral metabolism, whereas the other prodromes remain unexplained.

PRECIPITATING FACTORS

Considerable importance is generally attached to a number of factors said to precipitate an attack of arthritis in a patient with latent gout. Their true significance in relation to the disease has not

been determined, and it is difficult to evaluate how often they are chance associations.

Minor or major trauma has long been considered the commonest precipitating factor. The prevalent involvement of the large toes has been attributed to the chronic strain on these articulations sustained in walking or from the pressure of ill-fitting shoes. Many similar examples of injury as an antecedent to gouty arthritis can be cited.

The belief that certain foods are promotive of gout is one of the oldest medical traditions and is still accepted by a majority of competent physicians. The proponents of this theory contend that the ingestion of purine-rich articles by the gouty subject results in an accumulation of uric acid in the blood, thus inducing an acute attack of gout. Habitual dietary excesses are considered to be predisposing factors, whereas periodic indulgence supposedly serves as a precipitating force.¹² It is a most regrettable circumstance that these teachings, which are shrouded in the semisancity of a long and venerable heritage, have never been tested by either adequate experimentation or comprehensive statistical analysis of clinical data.

Because of the far-reaching practical importance of this question, the consideration of the relevant basic facts is recommended. Since predisposition to gout is inherited, it follows that dietary factors cannot be the cause of the disease. Although it is well proved that a high purine intake raises the blood uric acid content of a gouty subject, it has likewise been shown that neither hyperuricemia nor an elevated uric acid concentration in tissue fluids is by itself always sufficient to produce an attack of gouty arthritis, even in a predisposed subject. High-purine diets do not provoke the acute illness in latent gout with any regularity, and no correlation has been possible between the degree of hyperuricemia and the frequency, severity and duration of arthritis in gouty patients. It has been found that most gouty subjects do not show an adverse response to occasional excess-purine feedings, and that in well-controlled studies covering an extended period the frequency of seizures does not vary in alternating intervals of high-purine and low-purine intake. The incidence of gout among vegetarians is much higher than is usually assumed. The natural course of the disease is characterized by sudden changes in an erratic, unpredictable pattern. The temptation for both patient and physician to fasten the responsibility for these to some tangible factor is great, but the evidence quoted here should warn one against accepting as verified the influence of dietary habits on the development and progress of gout.

It has also been stated that certain foods, regardless of their purine content, are capable of produc-

ing regular attacks in some gouty patients, supposedly as an allergic manifestation. A specific brand of cheese or wine or a particular kind of fruit or vegetable has been held responsible. Similar observations have not been reported by other investigators.

Attacks have been observed subsequent to the institution of a ketogenic²¹ or high-fat diet. Lockie and Hubbard²² proposed that the latter be used as a provocative test.

Some clinicians consider the ingestion of alcohol to be the most important of all precipitating factors. Fermented beverages are thought to be much more provocative than is distilled liquor. Others hold the mode of use a significant circumstance, considering that persons who overindulge in meat habitually partake of red wine and malt liquors, and therefore sustain the combined effect of two inciting agents. All are agreed that certain gouty subjects fare sumptuously with some regularity and that some of their attacks follow dietary and alcoholic indiscretions. This sequence, however, does not usually exist. For example, one of the patients at the Massachusetts General Hospital experienced only two attacks in twenty years, although his excesses continued throughout the symptom-free interval. Another suffered ten attacks in ten years during middle life but none during the subsequent fifteen years while his habits of eating and drinking remained unchanged. Cases of this description are by no means exceptional, and serve to emphasize that the instrumentality of alcohol in precipitating gouty arthritis is unproved. Actually, chronic alcoholics²³ have been said to show no higher and totalers no lower than the average incidence. Only the collection of accurate data from a significant number of cases will give the final answer.

Attacks of gouty arthritis are said to have followed the intramuscular administration of liver extract and of salyrgan, ergotamine tartrate, insulin, decholin, thiamin chloride and other medicinal agents. The case reports are too sparse to allow a conclusion as to cause and effect.

Hench²⁴ has repeatedly stressed that gout should be suspected when arthritis occurs during the first seven days following a surgical procedure, but the exact incidence of postoperative gout is unknown.

Coincidental diseases such as leukemia, polycythemia and chronic glomerular nephritis, as well as marked blood loss and transfusions, are said to have activated latent gout. Furthermore, severe purgation, foreign-protein therapy, exposure to cold and dampness and emotional upsets have been accused of producing attacks.

COMPLICATIONS

As stated previously, premature vascular disease and the anatomic and physiologic alterations re-

sulting therefrom constitute the important complication of gout. Some earlier writers^{7, 23} have stressed the high incidence of venous thrombosis, a finding that has been rare in my experience.

The appearance of persistent albuminuria and casts usually marks the beginning of a vascular nephritis that may ultimately prove fatal. The majority of gouty patients die from uremia. Because of the frequency with which nephritis occurs in gout, Hench²⁵ states that chronic arthritis associated with distinct renal impairment suggests gout until proved otherwise. Some writers speak of secondary gout caused by chronic nephritis, other renal disease or leukemia. Such cases probably represent latent gout complicated by other diseases associated with hyperuricemia. Under these conditions, it is important to obtain a detailed family history and, if possible, blood uric acid determinations on the patient's relatives.

The incidence of urinary calculi in gouty subjects is relatively high, amounting to 12 per cent in Hench's²⁵ series. An occasional patient experiences one or more bouts of renal colic prior to the first gouty seizure. Arthritis in connection with urinary lithiasis should always suggest the presence of gout. No sound theoretical explanation for the frequent association of the two conditions is known, nor has the incidence of urate stones been determined.

Previously gout was assumed to be prevalent among lead workers, hence the term "saturnine gout." It, too, was considered an example of secondary gout due, in this instance, to the vascular nephritis of plumbism. Whereas gout is more rarely a complication of lead poisoning than was previously assumed,²⁶ it may of course be associated by chance with the vascular nephritis of plumbism. Other types of arthritis occurring in a patient with hyperuricemia due to renal damage from lead poisoning may in the past also have been erroneously diagnosed as gout.

Epicleritis due to urate deposits occurs rarely.^{5, 16} Eczema and various other complications are no more frequent than in all persons of comparable age and are probably unrelated to gout.

DIAGNOSIS

The diagnosis of joint diseases is in most cases relatively easy when based on a detailed medical history and a complete physical examination. A few well-chosen laboratory tests or a therapeutic trial with specific medication are often valuable adjuncts. Biopsies may be necessary. The passage of time and further observation are indispensable.

Clinical Findings

A history of recurrent attacks of acute arthritis separated by completely asymptomatic intervals should always suggest gout, particularly in a

middle-aged man. Provided the presence of the disease is suspected, confirmation in most cases is relatively simple. The abrupt onset of severe articular pain, usually without known cause, followed rapidly by a red, hot swelling of the joint, extending beyond the articular margins, is of great diagnostic significance, especially in a first attack. Additional aids are a positive family history, positive identification of tophi and the occurrence of cuticular desquamation as the edema subsides, a finding highly characteristic of gouty arthritis. The dramatic response to full doses of colchicine, rarely observed in any other types of arthritis, is of real diagnostic significance.

Laboratory Findings

Hyperuricemia is an almost invariable feature of the disease. Its presence, therefore, if not attributable to other causes, constitutes evidence of prime importance. The serum uric acid values are rarely lower than 6 mg. per 100 cc. In the few exceptions, less than 2 per cent, they vary between 5.2 and 5.8 mg.

For the determination of uric acid, one of two methods, that of Folin²⁷ or that of Benedict,²⁸ should be employed. Both depend on the reduction of complex tungstate reagents to colored compounds. This reaction is not strictly specific for uric acid and may be enhanced or inhibited by unrelated substances present in the blood. *While neither test offers undue technical difficulties, only the greatest care in preparing the reagents and frequent control determinations assure reliable results.* The use of serum is preferable to that of whole blood. Since the distribution of urates between the plasma and the cells is a function of the bicarbonate content, specimens should be collected and centrifuged under oil if the greatest accuracy is desired. Folin's²⁹ method for unlaked blood is free from the objections to the other whole-blood methods, but since it is doubtful whether diffusion of urates from the cells is ever complete, the method should not be used if sufficient blood can be obtained for a determination on serum.

No characteristic change in serum uric acid occurs immediately prior to an acute attack of gouty arthritis. In some cases it remains unchanged; in others it may be increased or decreased. *In order to avoid erroneous interpretations, particularly of response to therapy, it is extremely important to appreciate that the blood uric acid level is inconstant and that cyclic changes occur at irregular intervals.* In one case variations between 7.4 and 14.5 mg. per 100 cc. were observed that could not be attributed to any known cause and were in no way related to the incidence of arthritis.³⁰ Various tests³¹ designated to measure the urate-concentrating power of the kidney are neither entirely satisfactory nor necessarily of diagnostic value in gout.

Analyses of joint effusions in gouty arthritis reveal uric acid concentrations in the synovial fluid similar to those in serum¹⁵; the same is true for sugar. The viscosity is reduced and the protein content increased. The total leukocyte counts may vary from 1000 to 31,000, with polymorphonuclear leukocytes ranging from 50 to 95 per cent.

Patients with acute gouty arthritis generally have a mild to moderate leukocytosis. The mononuclear count is frequently increased. The sedimentation rate may be elevated. In several cases at the Massachusetts General Hospital the rates were as high as 2 mm. per minute (the upper limit of normal being 0.4 mm. per minute³²). Evidence of mild renal impairment is commonly met with. Achlorhydria occurs no more frequently in gouty patients than in other persons. An abnormal sugar-tolerance curve, occasionally present, is of no diagnostic significance.

Roentgenographic Findings

The roentgenographic findings most suggestive of gout are well-defined, punched-out areas, usually 5 mm. or more in diameter. They are most commonly observed in the subchondral bone at the bases or heads of the phalanges. The feet are apt to show these lesions even in cases in which they have never been affected clinically. Such changes may appear late in the disease; for example, 19 per cent of the patients in one series had had gout for twenty-eight years or longer and exhibited tophi and hyperuricemia in every case, yet failed to show subchondral lesions roentgenographically.²⁵ The frequency with which these defects, the result of urate deposition in bone, are found is directly related to the severity of the disease. They may be demonstrable in the region of joints not commonly affected—for example, in the neighborhood of the sacroiliac joint. They should be distinguished from the circumscribed areas of rarefaction seen in degenerative joint disease and rheumatoid arthritis. Similar findings may be produced by the gummas of syphilis and by leprosy and yaws, as well as by tuberculosis and Boeck's sarcoid. Occasionally tophaceous deposits result in bone expansion with or without destruction, thus simulating roentgenographically a bone tumor. In addition to such abnormalities, one may find thickening, joints of soft tissues, narrowing of conspicuous marginal overgrowth and marked destruction of the articular surfaces.

Decalcification occurs in a few patients who have suffered prolonged, severe attacks involving the small joints of the feet and wrists. In these exceptional cases, the marked decalcification, joint destruction and obvious ankylosis closely approximate the changes seen in specific infectious or rheumatoid arthritis. Premature arteriosclerosis

is frequently demonstrable in the vessels of the legs and feet.

Although the x-ray findings in gouty arthritis are characteristic and consistent, they cannot be considered specific. The roentgenologist's impressions should therefore be taken only as a corroboration of a clinical diagnosis.

Provocative Tests

Experience with provocative tests at the Massachusetts General Hospital has been most disappointing, whether these were applied immediately after an attack or during a remission. This has been true of a high-purine (2.5 to 3 gm.) diet or a high-fat (250 to 300 gm.) diet or of large amounts of port wine administered singly or in combination with the diets. Failure to precipitate an attack with any regularity has led to abandonment of these tests as diagnostic aids.

DIFFERENTIAL DIAGNOSIS

Occasionally gouty arthritis is confused with traumatic joint disease, cellulitis, rheumatic fever, one of the specific infectious arthritides, rheumatoid arthritis, Heberden's nodes or acute bursitis, particularly when the last is associated with a hallux valgus deformity.

Traumatic arthritis is as a rule readily diagnosed. Articular pain and swelling follow almost immediately on a known injury. Marked inflammatory reaction of the periarticular tissue is not discernible, and the symptoms always remain confined to the affected joint. The patient exhibits none of the characteristics of the gouty subject and his arthritis never responds to colchicine therapy. It should be remembered, however, that trauma may mark the onset of acute gout as well as that of infectious arthritis. In such cases differentiation is greatly aided by aspiration and analysis of the joint fluid. An acute traumatic effusion contains rarely more than 1000 leukocytes per cubic millimeter and polymorphonuclear leukocytes ranging from zero to 20 per cent, in contrast to the higher values usually found in the other acute arthritides.¹⁵

Cellulitis or septic inflammation is frequently suspected; in fact, it is sometimes diagnosed before it has become evident that one is actually dealing with acute gouty arthritis. Occasionally, the affected joints have been incised and drained. One can readily appreciate the diagnostic difficulties offered by a patient who presents himself with a painful, red, hot swelling of the dorsum of the hand or foot, with or without lymphangitis and fever. Failure to find a skin abrasion or other portal of entry for an invading organism and careful elucidation of the past history generally lead to the correct diagnosis.

Rheumatic fever, especially in young patients, can be simulated by recurrent attacks of gouty arthritis. The clinical differentiation, however, should not be difficult. The arthritis of rheumatic fever usually follows an upper respiratory infection or other precipitating factors by seven to fourteen days. Patients frequently exhibit weight loss, nosebleeds, skin eruptions, subcutaneous nodules, tachycardia and precordial pain. The electrocardiogram often shows a prolonged PR interval and other alterations. The ultimate development of valvular heart disease is of the utmost diagnostic importance.

Specific infectious arthritis, due to a pyogenic organism, in the acute phase more nearly resembles acute gouty arthritis than it does any other type of joint disease, particularly since it is occasionally recurrent. In such cases, usually caused by the gonococcus, the clinical picture shows some similarity to that of gout, as in a patient who entered the Massachusetts General Hospital suffering from his eighth attack of arthritis. He stated that recovery from the previous seven seizures had been complete. Differentiation was facilitated by a history of a genitourinary infection and such constitutional symptoms as chills and fever preceding in close parallelism every exacerbation of arthritis. Although the inflammatory swelling of specific infectious arthritis may be severe, it is rarely so marked or occurs so precipitously as does gouty arthritis. Particularly with the aid of synovial-fluid findings, one should not encounter serious diagnostic difficulties.

Typical rheumatoid arthritis ushered in by constitutional, vasomotor and neurologic symptoms, of insidious onset and characterized by symmetrical joint involvement, should rarely if ever be mistaken for gouty arthritis. In 18 per cent of all cases, however, rheumatoid arthritis is marked by an atypical onset, and in 7 per cent it may remain atypical for a long time. In this form, an apparently healthy person experiences an acute attack of arthritis without prodromes, preceding acute illness or an obvious focus of infection. The joint involvement may be polyarticular, migratory or, occasionally, monoarticular. Recovery from the first attack is often complete, and the remission may last for a few months or even for years. The patient may have a number of attacks before the disease becomes chronic. Careful clinical observation and determination of the blood uric acid concentration facilitate the distinction between the two diseases.

The clinical features of chronic gout with ankylosis may resemble even more closely those of rheumatoid arthritis. Two such cases have been

relatively early stage of the disease, and others have been reported.^{4, 23} In one,³⁰ the onset of gout at twenty-one years of age was followed by chronic arthritis within five years. Widespread ankylosis was demonstrable at the age of twenty-eight. The diagnosis of gout was confirmed by the identification of sodium urate crystals in tophi of the ear and in the fingers, olecranon bursa and tissues of four joints. Of particular interest were the findings in the astragalotibial joint. Extensive pannus formation, responsible for complete fibrous ankylosis, simulated strikingly the gross pathologic changes of rheumatoid arthritis. Even the microscopic appearance of the synovial tissues might have been difficult to distinguish definitely from the chronic inflammatory lesions of rheumatoid arthritis, except for innumerable small urate foci. Such unusual forms of gouty arthritis are admittedly rare. They should not be confused with rheumatoid arthritis. Clinical differentiation is greatly aided by a painstaking inquiry into the past and family histories. Biopsies of nodules, tophi and synovial tissues often lead to the correct diagnosis. Analysis of the synovial fluid may or may not help to distinguish one disease from the other. The association of the two is extremely rare. A few cases have been reported, but their authenticity is questionable.

Bursitis, particularly as a manifestation of a hallux valgus deformity, has probably on innumerable occasions been mislabeled as gouty arthritis. This diagnostic error can be avoided if the infected part is carefully examined. The swelling is limited to the bursa and the immediately adjacent tissues, and the distended sac may be easily palpated. Motions of the metatarsophalangeal joint are painless within a limited range.

Heberden's nodes, classic stigmas of degenerative joint disease, consist of hypertrophic osseous changes at the articular margins of the terminal interphalangeal joints. They are insidious in development and not usually productive of severe symptoms, and may be readily differentiated from tophaceous deposits in the skin and deeper tissues surrounding these joints. Occasionally, however, Heberden's nodes are acute in onset and are then frequently confused with gouty arthritis. The distal finger joints may be painful, reddened, bulbous, fluctuant and extremely tender. Numbness and tingling of the involved fingers may also be complained of. Heberden's nodes occur predominately in women and affect the index and middle fingers oftener than the other phalanges. Tophi, common in men and rare in women, are discernible by their yellowish color. It is well known, of course, that the two disorders may be associated coincidentally or casually.

SUMMARY

The varied manifestations of gout are reviewed in detail to acquaint physicians with the disease. If this treatise serves its purpose, there should result more correct diagnoses and fewer therapeutic errors.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**BENJAMIN CASTLEMAN, M.D., *Acting Editor*EDITH E. PARRIS, *Assistant Editor*

CASE 29401

PRESENTATION OF CASE

A fifty-one-year-old storekeeper was admitted to the hospital because of chest pain.

The patient was well until about five years before admission, when he noted the gradual onset of intermittent, substernal pain. The pain was variously described as being in the middle or just to the left of the sternum at the level of the third, fourth and fifth ribs and at times radiating to the left arm. It was unrelated to food, exercise or emotion but was sometimes intensified by deep inspiration. It lasted for a few minutes and was often followed by a feeling of discomfort for two or three hours. Sitting down occasionally relieved the pain. During the course of the next few years the pain increased in frequency and severity, so that on entry it was described as a dull, heavy sensation beginning at the lower end of the sternum, radiating to the left chest and occasionally to the left arm as far as the elbow, leaving the arm numb and heavy. The pain seemed to come on ten or fifteen minutes after he arose in the morning, persisted all day and went away one or two hours after he retired at night.

During the year or two before admission, the patient had had "considerable gas in his stomach" following meals, which was relieved by belching. There were some lower abdominal cramps and diarrhea without blood or mucus for a period of four or five weeks. He was seen by various physicians one of whom had performed gastrointestinal and gall-bladder x-ray studies and had told him that he had "colitis" and a misshapen gall bladder. The diarrhea ceased, but the abdominal discomfort continued. It was sometimes relieved by soda or a glass of whisky, and at times aggravated by eating.

About six months prior to entry, the patient developed a severe cough and wheezing dyspnea. He lost his voice for a short time. The cough was "tight" and worse in the mornings. On one occasion he raised bright-red sputum every morning for about a week. At other times however, the sputum, which was copious in the mornings, was whitish to brownish but not foul. It seemed to

increase with exertion. During that time, he felt tired but had no chills, fever or night sweats. He had lost 10 to 20 pounds in the course of the year and a half preceding entry. His appetite had remained fair, and he was able to eat "nearly everything." There was no vomiting, dysphagia or diarrhea, but he had had a feeling of nausea occasionally at night. The patient had no orthopnea but slept on two pillows to prevent coughing. He had noted the gradual onset of dyspnea on exertion, which persisted. For the two months before admission he had received two digitalis capsules daily, without improvement. All his symptoms were variously described as progressive or intermittent, with periods of remission and exacerbation. There was no history of aspiration of a foreign body or of operation on the nose, mouth or pharynx.

Physical examination showed a slightly obese man in no distress. The anteroposterior diameter of the chest was increased with somewhat diminished respiratory excursions, which seemed to be mainly diaphragmatic. The left half of the diaphragm was slightly higher and moved less than the right half. One or two observers noted a questionable dullness with diminished tactile fremitus and breath sounds at the left base, whereas two or three others thought that the lungs were clear. The left border of cardiac dullness was 10 cm. to the left of the sternum. The sounds were of good quality and regular. The aortic second sound was greater than the pulmonic. There were no murmurs. The examination otherwise was negative.

The blood pressure was 125 systolic, 85 diastolic. The temperature was 98.6°F., the pulse 84, and the respirations 32.

The blood showed a red-cell count of 5,730,000 with a hemoglobin of 18.5 gm. The white-cell count was 10,300, with 60 per cent neutrophils. The urine was normal. The stools were guaiac negative. A blood Hinton test was negative. The blood protein was 7.3 gm. per 100 cc. A Graham test was negative. An electrocardiogram revealed a rate of 90, a PR interval of 0.14 second and slight axis deviation. The T waves in Leads 1, 3 and 4 were low, and T₄ was slightly diphasic. X-ray examination of the chest showed a mass behind the heart on the left side with sharp medial and anterior borders, apparently corresponding to a collapse of a large portion of the left lower lobe. The left hilus was slightly smaller than normal. There was no respiratory shift of the mediastinum. The heart was normal in size and shape. A gastrointestinal series showed the esophagus crossing the mass in the left lower chest without being attached to it. On re-examination, however, a herniation of the cardiac portion of the stomach

*On leave of absence.

through the diaphragm was noted (Fig. 1). The stomach was apparently curled on itself as it passed through the opening so that only with the

see the film that was described in the history, but in which I could not find or recognize the shadow noted on the left side "with sharp medial and



FIGURE 1. *Roentgenogram following Barium Meal.*
Note the hiatus hernia and the round mass above the fundus of the stomach.

head depressed and the patient lying on his back was the entire supraphrenic mass filled with barium. A barium enema was negative. There was no evidence of herniation of the large bowel through the diaphragm. The splenic flexure approached the diaphragm somewhat more closely than usual and moved freely with respiration.

During the first few days after admission the patient had several attacks of coughing, as well as a slight dull pain just to the left of the lower end of the sternum and considerable gas pain.

An operation was performed on the eighteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. JOHN W. STRIEDER*: Perhaps we might see the x-ray films first. I should particularly like to

anterior borders, apparently corresponding to a collapse of a large portion of the left lower lobe.

DR. LAURENCE L. ROBBINS: This presumably is the solid mass described in the lung, and these air bubbles represent the hernia. I should say that this line demonstrates what they were trying to bring out for the medial margin of the lesion in the chest. So far as the spot film is concerned, this is the esophagus, and this the stomach; there still appears to be an area of increased density above the fundus. I do not believe that the splenic flexure is abnormal in position in the film of the colon.

DR. STRIEDER: Do you think you can see in any of the films an area that is consistent with a collapsed portion of the left lower lobe?

DR. ROBBINS: I cannot see a definite area of collapse. There is an area in the left lower lobe

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in which there is no air. I should think that this was its margin, with the hernia below it, because one can see a bubble. This film again shows a gas bubble in the herniated portion of the stomach. It is perfectly possible that the mass above it is in the lung.

DR. STRIEDER: Are you impressed by the pulmonary shadow itself?

DR. ROBBINS: I do not know exactly what to say. It is quite a sharply defined shadow for a hernia and it certainly seems to be surrounded by air, which would make one think it was within the lung or against the pleura.

DR. STRIEDER: We have a fifty-one-year-old man on whom an x-ray diagnosis of esophageal hiatus hernia of the stomach had been made. As I looked this over, I thought I could reconcile the symptoms with the x-ray diagnosis, which is often dangerous. There are several aspects that do not fall in line, however, and perhaps I shall devote a moment or two to these as I come to them.

In the first place, symptoms of five years' duration in a fifty-one-year-old man are not unusual for esophageal hiatus hernia or for any type of diaphragmatic hernia. Although the hernia may be present at birth, the symptoms may not occur until the patient is well along in years. It is interesting that the first diagnosis by x-ray of esophageal hiatus hernia was made at the Mayo Clinic in 1921. In 1940, Harrington* published a series of 250 cases of diaphragmatic hernia, of which 198 were paraesophageal in type. So it is by far the commonest type of diaphragmatic hernia recognized.

The pain that was variously described as being in the middle or just to the left of the sternum, radiating to the left arm, is explainable, in so far as pain in the arm is concerned, on the basis of phrenic reference due to diaphragmatic spasm. In diaphragmatic hernia, pain commonly simulates that of angina, or at least is thought to simulate that of angina. Patients may complain of severe pain in the arm in connection with their thoracic pain. Classically, paraesophageal hernia pain radiating through to the back and to the left of the spine is usually lower, but any patient may have a variety of symptoms depending on the type of hernia, the quantity of viscus herniated and the type of viscus herniated.

"Sitting down occasionally relieved the pain." That is contrary to the usual story. Most patients with esophageal hiatus hernias are relieved when they stand up or are propped up in bed because the upright position tends to reduce the hernia, if it is reducible.

"During the year or two before admission the patient had had 'considerable gas in his stomach' following meals, which was relieved by belching." This again is classic for diaphragmatic hernia. There is trapping of air above the diaphragm, causing considerable distress, and relief by belching. Consequently many erroneous diagnoses are made. Cholecystitis is a diagnosis often made when the patient's symptoms are entirely due to diaphragmatic hernia.

I cannot explain the lower abdominal cramps and diarrhea on the basis of gastric herniation alone. It is possible that at the time of these episodes the patient may have had a portion of the colon in the hernial sac, although that was never demonstrated in the films. "The diarrhea ceased, but the abdominal discomfort continued. It was sometimes relieved by soda or a glass of whisky, and at times aggravated by eating." That again is unexplainable, but apparently homely remedies do wonderful things for patients. The fact that the pain was relieved by whisky reminds me of a physician of this hospital whose symptoms were relieved by whisky although he had an ulcer of the stomach that was about to perforate when demonstrated at operation. Of course, the relief from soda seems reasonable. Patients with hernia through the diaphragm have distress because they regurgitate gastric secretions into the lower esophagus, and ulceration of the lower esophagus frequently occurs on the basis of prolonged, continued regurgitation. They often have ulceration of the stomach from the pressure of the hernial orifice on the wall of the stomach. This may give rise to hematemesis or to frank blood, or more commonly occult blood, in the stools.

"About six months prior to entry, the patient developed a severe cough and wheezing dyspnea. . . . On one occasion he raised bright-red sputum every morning for about a week." That is the ruby-hued herring that upsets our tight little argument. I have never seen a patient with diaphragmatic hernia who coughed up blood, and I find no reference to this in the 198 cases that Harrington observed at the Mayo Clinic. It is entirely conceivable, however, that the cough, dyspnea and other respiratory symptoms are explainable on the basis of hernia. We know that there is a certain amount of diaphragmatic spasm and crowding of the lung by the hernia if it is sufficiently large, which will result in shortness of breath and even wheezing. The site of the hernia makes it seem unlikely, at least to me, that the hernia could have so encroached on the lung that there was actual distortion of the bronchus to account for the cough and bloody sputum. There is no mention of bronchoscopy. If the pulmonary

*Harrington, S. W. Diagnosis and treatment of various types of diaphragmatic hernia. *Am J Surg.* 50:381-446, 1940

symptoms had been of significance I think it would have been suggested and perhaps carried out. It would have been interesting to know about it, at any rate. The other alternative, of course, is to consider whether the patient vomited the bright-red blood, rather than coughed it up, which would fit nicely into the picture, but would not explain the prolonged cough and the copious sputum unless they were caused by the emphysematous changes of advancing years.

A weight loss of 10 to 20 pounds can well occur in a patient with esophageal hiatus hernia. These patients develop a "food fear" and because of this fear or the inability to take food they lose weight. The patient stated that he was able to eat nearly everything, but closer questioning might have elicited the fact that he was on a reasonably restricted diet. There is no question that there is such a thing as a so-called "stomach cough," which we heard a great deal about years ago in the early days of sanatoriums and is still spoken of in tuberculosis institutions. Many tuberculous patients on prolonged bed rest have gastric symptoms related to hyperacidity, and with it they have a cough that is relieved when the hyperacidity is controlled. I am convinced that coughing in such cases is some sort of a reflex phenomenon since we see it clinically so often.

"All his symptoms were variously described as progressive or intermittent, with periods of remission and exacerbation." That again is typical of hiatus hernia. These patients may be perfectly well for months, during which time the stomach is in normal position. The prolonged symptoms are probably due to the adherence of the stomach in the hiatus, or its being retained there for a period of time. The patient had no history of aspiration of a foreign body or anything else to make us suspect a suppurative lesion in the lung that caused cough.

The stools were negative, although commonly with diaphragmatic hernia the stools are positive for blood because of prolonged bleeding from an erosion of the stomach, which often results in secondary anemia. Which brings me down to the point where I must make a diagnosis.

Was a bronchoscopy performed?

DR. BENJAMIN CASTLEMAN: No.

DR. STRIEDER: I do not see how I can go any farther than to say that this patient had a diaphragmatic hernia. I am not very much impressed, and I gather that Dr. Robbins is not, by the pulmonary shadow. I think that the shadow might have been due to compression of the lung.

DR. ROBBINS: Now that I have had more time to look at the gastrointestinal film, I believe that I can see a round mass above the barium-filled fundus of the stomach.

DR. STRIEDER: It is not part of the hernia?

DR. ROBBINS: I do not believe so, since it is more or less completely surrounded by air, and apparently is separate from the upper limit of the fundus of the stomach.

DR. STRIEDER: There is room for all sorts of conjecture. I cannot explain the hemoptysis on the basis of anything that we have to go on except the possibility, as Dr. Robbins has pointed out, of tumor in the lung. Given an x-ray diagnosis of a tumor in the lung, there is a certain differential diagnosis that one can go through, but actually it resolves itself into a more or less philosophic discussion concerning the exact histopathology, and the pathologists often surprise us when they tell what it is. If we can accept this shadow as evidence of a pulmonary tumor, then we have to make such a diagnosis. However, I think I shall be brash, fly in the face of the X-ray Department and refuse to be impressed by it, although that may be a serious error. Probably all these symptoms can be explained on the basis of diaphragmatic hernia of the paraesophageal type.

CLINICAL DIAGNOSIS

Esophageal hiatus hernia.

DR. STRIEDER'S DIAGNOSIS

Esophageal hiatus hernia.

ANATOMICAL DIAGNOSES

Esophageal hiatus hernia.

Bronchiogenic cyst of lung.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Dr. Robert K. Brown operated on this patient. Since he is not here I shall read part of his operative note:

Under intratracheal ether anesthesia, a long, curved, posterolateral incision was made over the left ninth rib, and approximately 35 cm. of this rib was subperiosteally resected. Free pleural space was entered. There was a herniation in the posterior leaf of the diaphragm about 7 cm. in diameter. This was somewhat adherent to the lower lobe of the left lung. As the adhesions were separated and the lung mobilized from the diaphragm, it was found that, on the medial aspect of the basal segment of the lower lobe, a rounded, tense, 4-cm. mass presented. This seemed to be connected to a cystic mass that occupied most of the basal segment of the left lower lobe. Running from it through the diaphragm between the hernia and the esophageal hiatus were two good-sized vascular structures, one about 2 mm. in diameter, and the other about 5 mm. in diameter and rather thick walled. These were dissected free, doubly ligated and cut. They turned out to be veins, the larger having a mural thrombus in its lumen. The remainder of the basal lobe was readily freed.

It was then apparent that there were two lesions—the diaphragmatic hernia, which was easily reducible, and the cystic tumor in the lower lobe, which was thought to be a bronchiogenic cyst. It was decided to repair the hernia and remove the cyst. Since

nate from ordinary bronchiectasis. Most lung cysts are certainly of bronchial origin.

Although the preoperative diagnosis was hiatus hernia, there were several men who continually



FIGURE 2. Photograph of Bronchiogenic Cyst.

segmental lobectomy is not an absolutely clean procedure, it was also decided to repair the hernia by imbrication without opening the diaphragm. This was done, and a good approximation of normal strong diaphragm was obtained, the suture line running posterolateral in a radial direction. Mass removal of the basal segment of the left lower lobe containing the tumor was carried out.

asked the X-ray Department whether this lesion was in the lung.

DR. ROBBINS: With reason, I should say.

CASE 29402

PRESENTATION OF CASE

The specimen that we received was a segment of lung containing the large cystic mass that Dr. Brown was able to feel. After fixation, section of the mass revealed a large cyst filled with gelatinous fluid (Fig. 2). Microscopic examination of the cyst wall showed it to be lined with ciliated bronchial epithelium and to contain foci of smooth muscle and cartilage. It was therefore a true bronchial cyst within the lung. Most people believe that these cysts are congenital in origin—in other words, that in the embryologic development of the lung one of the lung buds fails to develop and the bronchial secretion is unable to get out. Although we were unable to find any communication with a large bronchus, I imagine there must have been one with a small bronchus; otherwise the patient would not have coughed up blood. There was no inflammatory reaction around the lesions. Such absence of infection is often used as an argument against the theory that lung cysts origi-

A sixty-three-year-old tobacco farmer was admitted to the hospital because of pain and weakness in the right arm.

The patient had been in apparent good health until about ten months before entry when he noted pain and weakness of the upper arm that bothered him while working. The pain increased in severity until seven months before entry, when it occurred at night and was relieved by letting the arm hang down. Chest roentgenograms at a community hospital about four months before admission were said to have shown a mass in the right upper chest. He was given a course of seven x-ray treatments over a month's time with apparently no decrease in the size of the mass. While receiving the x-ray treatments he had a paroxysmal nonproductive cough, which cleared after treatment. The pain and weakness in the arm increased in severity. The pain was in the lateral aspect of the right deltoid region, the bi-

ceps, the extensor surface of the forearm and the right ring finger. It was aggravated by lifting and by certain positions in bed. In the month before entry he developed a deep soreness in the right side of his neck. There was no weight loss, anorexia, hemoptysis, dyspnea, orthopnea, headache, giddiness or changes in the voice.

At twelve years of age "a large swelling of the

ward rotation of the right arm. There was no noticeable atrophy, masses, hyperesthesia, numbness or vascular changes.

The blood pressure was 110 systolic, 70 diastolic. The temperature was 98.6°F., the pulse 70, and the respirations 20.

The blood showed a red-cell count of 5,140,000, with a hemoglobin of 15.3 gm. The white-cell



FIGURE 1. Roentgenogram of Chest.

The mass in the right superior mediastinum lies between the trachea and esophagus. There is slight extension to the left, above the aortic arch.

neck had been drained through a midline incision." He had had typhoid fever at twenty. About twenty years prior to admission it was discovered that he had diabetes, which was controlled by diet without insulin.

Physical examination showed a weatherbeaten man in no distress. Both pupils were small and reacted to light and accommodation. The trachea was deviated to the right. No masses or lymph nodes were palpable. There was tenderness to deep pressure over the muscles in the posterior triangle of the neck. The chest was barrel shaped. The heart and lungs were normal. The shoulder motions were normal except for limitation of out-

count was 4200, with 75 per cent neutrophils. The urine showed a + test for albumin, but was otherwise normal. The blood sugar was 94 mg. per 100 cc.

X-ray examination of the chest showed a mass arising from the upper mediastinum and lying between the trachea and esophagus (Fig. 1). The mass measured approximately 13 by 13 cm. It was largely on the right side but there was apparent extension to the left. It was attached to the trachea, which was displaced to the left and posteriorly. It was probably attached to the esophagus in the region of the aortic arch. There were no pulsations. The mass appeared to change its

shape on deep inspiration and slightly on changing position. There was no shift of the mediastinum. The lungs were normal. The heart was slightly enlarged in the region of the left ventricle. The aortic arch was prominent. The diaphragm showed normal respiratory motions. The visualized bones appeared normal.

On the fifth hospital day a mediastinal exploration was performed.

DIFFERENTIAL DIAGNOSIS

DR. REED HARWOOD: Our problem is a discussion of a mass in the chest and the nerves involved by this mass.

Taking the second part first, the nerves involved appear to be the medial brachial cutaneous and the intercostohumeral on the medial side of the biceps.

These are supplied by the first and second thoracic nerves. The dorsal antibrachial cutaneous and the medial antibrachial cutaneous are the sensory nerves of the dorsum of the arm. The first of these is supplied by the fifth to the eighth cervical, and the second by the eighth cervical and the first thoracic. The ulnar nerve, which is the one involved so far as the finger is concerned, is supplied by the eighth cervical and the first thoracic. The area over the deltoid region is supplied by the supraclavicular nerve, which comes from the third to the sixth cervical nerve. It is hard to explain on the basis of a chest tumor how the patient had so much pain over the deltoid region since these nerves arise outside the thoracic cage. Similarly, the description of weakness of the arm and limitation of motion of the shoulder joint, particularly on outward rotation, I cannot explain on the basis of a lesion in the chest, because these muscles are supplied by nerves higher in the cervical region.

I shall discuss the mass that was drained at the age of twelve. I suppose that it was a thyroglossal cyst and not connected with the present illness, unless we can reason that a patient who had one embryonic rest is apt to have another elsewhere.

There are two discrepancies that I want to point out. The first is that in the physical examination the trachea was said to deviate to the right, and in the x-ray description the trachea was said to deviate to the left. The other discrepancy is that the record states at one point that the tumor arose between the esophagus and trachea and at another point that the tumor had pressed the trachea backward as well as to the left. I am going to ask Dr. Robbins to straighten me out on these two points. It does not seem possible for a tumor arising between the trachea and esophagus to press the trachea posteriorly.

DR. LAURENCE L. ROBBINS: If the record states that the trachea was deviated to the left, it is incorrect. I remember the case very well. The trachea was in the midline and was displaced anteriorly; the mass lay between the trachea and esophagus and pressed against both. It was attached to the trachea because the mass moved each time the patient swallowed.

This is the mass, chiefly on the right but with extension to the other side. The mass was smooth so far as could be determined from the films. As I said before, it was in the midline and pushed the trachea anteriorly, not posteriorly.

DR. HARWOOD: The mass is said to have changed in position.

DR. ROBBINS: That may have been a faulty observation. I examined the patient and was convinced at the time that the mass changed its shape with changes in his position.

DR. HARWOOD: Dr. Robbins evidently thought it was a cyst before operation and is now not quite so sure.

DR. ROBBINS: That was my impression.

DR. HARWOOD: There are a number of masses in the chest that I am going to exclude before considering tumors of the mediastinum. Tuberculosis and empyema can be excluded on the basis of the history. Lung tumor can be excluded because of the absence of cough and hemoptysis. Thymoma can be excluded because such tumors arise in the anterior mediastinum, and there is no evidence of myasthenia gravis. I am going to exclude lymphoma because of apparent lack of response to x-ray treatment. Because there was no tracheal tug or vascular phenomena in the arms, aneurysm seems unlikely, but one should be sure that the Hinton test was negative.

DR. BENJAMIN CASTLEMAN: The Hinton test was negative.

DR. HARWOOD: Malignant disease can be excluded less certainly, but I am inclined to think that this was not a malignant tumor, principally because the tumor was perfectly round and there were no constitutional symptoms, such as weight loss. However, I cannot exclude the possibility of a benign tumor that had become malignant.

In considering mediastinal tumors I shall mention the esophagus first. A tumor of this size in the lumen or in the wall of the esophagus would certainly cause dysphagia, which this patient did not have. Of the cystic embryonic rests, dermoid cyst is one of the more frequent ones, but it usually arises in the anterior mediastinum and often areas of calcification are seen in the x-ray films. I think it is not likely that this was a dermoid cyst. Bronchiogenic and tracheal cysts are both good possibilities. The location is correct, and such tu-

mors may be soft. A solid embryonic rest, such as a teratoma, is usually irregular in outline and shows areas of calcification. Regarding tumors of neurogenic origin, von Recklinghausen's disease may present a single tumor arising in the neural canal. This usually produces erosion of the articular facets of the vertebrae in that region, but I take it that such a lesion was not present here. Furthermore, there were no other neurofibromas noted on physical examination. A single neurofibroma of the mediastinum is another possibility. They usually arise in the posterior mediastinum and produce erosion of the ribs.

Finally, we should consider the possibility of substernal goiter. Against this is the fact that there were no masses in the neck. Most substernal goiters, not all of them, are attached to the lower pole of the thyroid. Furthermore, 90 per cent are seen in front of the trachea rather than behind it. So there is a 10 per cent chance, anatomically speaking, that it was in the correct position. In substernal goiter the enlargement is preponderant on one side and the trachea is deviated to the opposite side. The deviation begins at the hyoid bone and obtains maximal deviation at the widest part of the tumor. Since in this case there was no deviation of the trachea, I am going to say that this patient did not have substernal goiter. I am therefore led to the conclusion that he had a cyst of the trachea, possibly a bronchiogenic cyst, and that is my final diagnosis.

DR. JOST MICHELSEN: Were there no x-ray films of the cervical spine?

DR. RICHARD H. SWEET: I do not recall. At any rate, none were taken here. He had been studied extensively at a good clinic in Connecticut. His presenting symptom then was pain in the arm and shoulder girdle. There was no suspicion of a mediastinal tumor, but a film of the shoulder showed a half-moon shadow that suggested tumor, and a chest plate was obtained.

DR. MICHELSEN: The description of pain suggests involvement of the sixth and seventh nerve roots on the right.

DR. SWEET: What sort of lesion would explain that?

DR. MICHELSEN: I am not prepared to say. I am just suggesting that the distribution of the pain sounds more like root than peripheral pain.

DR. SWEET: Do you think it likely to be caused by a tumor in the chest?

DR. MICHELSEN: No; that is why I asked if x-ray films of the cervical spine had been taken.

DR. SWEET: I do not believe that the symptoms, other than the cough, were caused by the tumor.

I do not recall what I put down as my preoperative diagnosis, but Dr. Robbins and I finally concluded that it was a cyst of some kind. We considered neurofibroma.

It turned out to be a solid tumor but one of soft consistence. The x-ray films had localized it exactly; it was adherent to the trachea and had to be separated from the esophagus. Only a portion of the tumor was between the two organs, the majority of it protruding into the right side of the chest posteriorly, not anteriorly. As I freed it from its pleural covering and dissected it free, it looked like a goiter. As I followed it up I could see that its real attachments, as judged by vascular connections, were coming from the neck. I finally developed it down to a rather broad pedicle, which was obviously the lower pole of the thyroid gland, not a substernal goiter but a posterior mediastinal one. There was no evidence of goiter in the neck. The mass was so large that it could not have been removed from above.

CLINICAL DIAGNOSIS

Mediastinal cyst.

DR. HARWOOD'S DIAGNOSIS

Tracheal cyst (? bronchiogenic).

ANATOMICAL DIAGNOSIS

Colloid goiter.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Microscopic sections confirmed the diagnosis of colloid goiter.

DR. WILLIAM B. BREED: How do you explain the symptoms?

DR. SWEET: I do not. The only symptom that the tumor caused was the cough.

DR. MICHELSEN: What about the pain? Did it continue to bother him?

DR. SWEET: At the time of discharge, the patient said that it was improved, but not completely.

It was my impression that the pain was due to a bursitis or to a cervical arthritis or something of that sort. At a subsequent follow-up visit, however, he was in an excellent state of health. Although there was still a certain amount of stiffness of the arm at the shoulder, he was completely relieved of pain.

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STREPTOCOCCUS SORE THROATS AND SCARLET FEVER

DURING World War I many studies of scarlet fever and other streptococcal infections were made in the United States Army camps. Considerable information was acquired concerning the significance of these infections and their mode of spread. Since that time, the general use of the Dick test as a measure of susceptibility to scarlet fever and the classification of streptococci into specific groups and types have made possible more intelligent and more precise epidemiologic studies, and have served to clarify the relation between scarlet fever and other hemolytic streptococcus infections of the

upper respiratory tract. The application of this knowledge to recent studies of scarlet-fever outbreaks in Army camps has thrown further light on this important subject. This, in turn, has served to bring into focus certain inconsistencies in the public-health attitude toward these infections, which deserve reconsideration in the light of present-day knowledge.

Schwentker,¹ in a recent report of a commission established by the Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, presented a survey of hemolytic streptococci in certain Army camps. At three of the posts in which the commission's investigation was carried out there were only sporadic cases of scarlet fever, but at another post an epidemic of this disease occurred. The results of these studies are of interest and serve to corroborate the impressions gained in many other similar studies carried out in this country and in England and Germany since the introduction of the serologic classification of streptococci into Griffith's agglutinative types.

Briefly, Schwentker and the other members of the commission concluded from their studies that during an epidemic of scarlet fever most of the cases are caused by a single type of streptococcus. This type also represents a high percentage of the strains recovered from normal carriers. During endemic periods, on the other hand, no single strain predominates among the streptococci causing scarlet fever, a number of types usually being involved. These types are also found in normal carriers but they do not predominate over the other nonscarlatinal strains. They also found a definite relation between the gross streptococcus-carrier rate and the incidence of scarlet fever. The same relation held for the Group A (human virulent) streptococcus-carrier rate, as well as the carrier rate for the scarlatinal types. The changes in the gross carrier rate were due primarily to variations in the carrier rate of virulent Group A strains, and these in turn depended on changes in the rate for the carriers of the scarlatinal type.

During an outbreak of scarlet fever in a given ward these investigators found that the scarlatinal

strain of streptococcus becomes distributed throughout the occupants of the ward to a varying degree. Depending on the degree of this distribution, it fails to reach a certain proportion of the men and they naturally remain well. Among those who come in contact with the scarlatinal strain some are resistant to the organism, presumably because of an antibacterial immunity. Regardless of their Dick reactions they remain well, and either promptly eliminate the streptococcus or become carriers. Those without bacterial immunity develop evidence of clinical infection. The Dick-positive patients, that is, those who are susceptible to the toxin, develop scarlet fever, whereas those who are Dick negative have streptococcal tonsillitis without a rash.

A second clinical and epidemiologic study of an explosive outbreak of streptococcal sore throat in an army camp was recently reported by Bloomfield and Rantz.² A total of 341 cases occurred within a period of five days, and about 83 per cent of them began in the first two days. In approximately one fourth of all these cases there was a classic scarlatinal rash, which ran the usual course with eventual desquamation. In other patients there was only a trace of exanthem, and in the majority a rash was not seen at any time. However, there was no clinical indication that the patients with a rash were suffering from a disease that was in any other way different from that of the men without a rash.

These workers raise the question whether the use of the term "scarlet fever" with the implication of its fundamental difference from "acute tonsillitis" does not serve to maintain confusion and diagnostic quibbling. They believe that the entire group should be referred to as streptococcal sore throat (with or without associated scarlatinal rash). They also think that the same rules for isolation and quarantine should hold for all these cases, regardless of whether or not a rash occurs.

At the present time health departments throughout the country quarantine "scarlet fever" but not "tonsillitis," and this, according to Bloomfield and

Rantz, shows a complete misunderstanding of the subject. In Massachusetts and in many other states not only does this incongruity persist, but there are differences in the isolation and quarantine periods within adjacent subdivisions of the same state. It would be well for the state and local health departments to reconsider this problem at the present time with a view to bringing their regulations in accord with present knowledge concerning this group of infections, and take the same opportunity to standardize isolation and quarantine regulations.

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HIERONYMUS FABRICIUS

FABRICIUS is best known as the teacher of Harvey. About 1600, Harvey attended the medical school at Padua, where Fabricius taught anatomy. It was there, in the old anatomical amphitheatre, which is still in existence, that Harvey heard for the first time, when attending one of the candle-light lectures of this famous teacher, a description of the valves of the veins. Fabricius was the first to demonstrate them publicly, and there seems to be little reason to doubt the inspiration Harvey received, to use Osler's phrase, from "the most distinguished teacher of the time, in the most distinguished school of Europe." The anatomical description and the function of the veins, as disclosed in Fabricius's lectures, stimulated Harvey to discover the circulation of the blood. He received at the same time an impetus to study embryology, a subject later to be markedly influenced by one of his books.

Two treatises by Fabricius, one on the formation of the egg and of the chick and the other on the formed fetus, have long remained buried in "that most excellent preservative, the Latin language." Dr. Howard B. Adelmann,* professor of histology

**The Embryological Treatises of Hieronymus Fabricius of Aquapendente: The formation of the egg and of the chick (De Formatione Ovi et Pulli) and the formed fetus (De Formato Foetu).* A facsimile edition, with an introduction, a translation and a commentary by Howard B. Adelmann, Ph.D. 883 pp. Ithaca, New York: Cornell University Press, 1942.

and embryology at Cornell University, has translated these into English, with the addition of a brief biography of Fabricius, an essay on embryology before the time of this great anatomist, an analysis of the treatises and a bibliography of the known editions. The translations are given in full, and facsimiles of each work are reproduced; there are numerous notes and commentaries, a list of references and an excellent index. This publication is one of the recent outstanding scholarly productions in the history of medicine. Furthermore, the book, published by the Cornell University Press, is a superb example of the work of a modern press.

Fabricius's position in embryology is not particularly easy to assess. It is correct to refer to him as the most distinguished teacher of his time, and as Adelman has pointed out, the embryologic treatises represent no mean achievement. In fact, some believe that they are of even greater anatomical importance than his work on the valves of the veins.

Fabricius lacked, as did most of his contemporaries, what Singer has called "complete speculative freedom." Needham was, moreover, impressed by Fabricius's "genius for exsuccous and formal discussions." Osler wondered how Fabricius, a teacher of wide learning and remarkable powers of observation, "could have been so blinded as to overlook the truth which was tumbling out, so to speak, at his feet." Dr. Adelman believes that Fabricius's faults, particularly his subservience to authority, were probably unavoidable—"a fault Fabricius shared, not only with Vesalius who preceded him, but also with many who came after, even Harvey. He adds: "The basic explanation, moreover, is not far to seek. We are all children of our times; we all see with the eyes of the centuries that have preceded us; truth dawns but slowly on the human mind."

MEDICAL EPONYM

GRADENIGO'S SYNDROME

Giuseppe Gradenigo (1859-1926), professor of ophthalmology at Turin, published a paper entitled

"Über circumscribte Leptomeningitis mit spinalen Symptomen und über Paralyse des N. abducens otitischen Ursprungs [Circumscribed Leptomeningitis with Spinal Symptoms and Paralysis of the N. abducens of Otitic Origin]," which appeared in the *Archiv für Ohrenheilkunde* (62: 255-270, 1904). A portion of the translation follows:

There exists a peculiar symptom complex in the association of acute otitis media (with or without reactive mastoiditis) and isolated paresis or paralysis of the N. abducens on the side corresponding to the aural lesion, and without the occurrence of other local or general signs of disease. . . . The syndrome under discussion is characterized chiefly by three symptoms, which are intimately related to one another and which ordinarily are complained of by the patient himself: acute inflammation of the middle ear, persistent pains in the temporal and parietal region and paralysis of the N. abducens.

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DEATHS

DASCOMBE — OTHO L. DASCOMBE, M.D., of Waltham died September 26. He was in his sixty-fourth year.

Dr. Dascombe received his degree from Johns Hopkins University School of Medicine, in 1905. Following in ternship at Waltham Hospital, he was appointed a staff member in 1918. He was a fellow of the Massachusetts Medical Society and a member of the American Medical Association.

A sister and a brother survive.

LELAND — GEORGE A. LELAND, JR., M.D., of Brook line, died September 22. He was in his fifty-eight year.

Dr. Leland received his degree from Harvard Medical School in 1911. He then became house officer at the Massachusetts General Hospital and was associate surgeon there at the time of his death. He was a member of the staff of the Collis P. Huntington Memorial Hospital, associate surgeon of the Palmer Memorial Hospital, consulting surgeon of the Massachusetts Eye and Ear Infirmary and of the Addison Gilbert Hospital in Gloucester and a member of the staff of the New Hampshire Memorial Hospital at Concord. He had been instructor for fifteen years at Harvard Medical School.

He was a member of the Massachusetts Medical Society, the American Medical Association, the American Surgical Association, the American College of Surgeons, the New England Surgical Society, the New England Cancer Society and the New England Obstetrical and Gynecological Society.

His widow, his mother and a daughter survive.

BOOK REVIEW

Renal Lithiasis. By Charles C. Higgins, M.D. 12¹/₂ cloth, 140 pp., with 18 illustrations. Springfield, Illinois: Charles C Thomas, 1943. \$3.00.

This short monograph is based on the Beaumont Lectures on Renal Lithiasis, delivered by the author. More than half the book deals with a discussion of the etiology of renal stone and of its relation to faulty diet and vitamin A deficiency. Included in this chapter is the technique of stone analysis. This is followed by a brief review of the surgical management of cases of renal stone. A short chapter on the dietary treatment and prevention of kidney stones, with a list of sample diets, concludes the book.

The book is far too elementary to be of value to the established urologist. The chapter on surgical management is sketchy, and the discussion on the dietary treatment and prevention of kidney stones will remind the average surgeon of the limited success he has had with this form of therapy.

From the student's point of view, the survey of the literature on the etiology of renal lithiasis suffers by being far too biased in favor of dietary imbalance and vitamin A deficiency as the main causes of renal stone. There are many significant papers that point to the incompleteness of the evidence for such a concept of stone formation in the experimental animal, and the relation of diet to the formation of renal stones in man is even more tenuously established.

(Notices on page x)

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GLOBAL MALARIA*

BRIGADIER GENERAL JAMES STEVENS SIMMONS, M.C., A.U.S.†

WASHINGTON, D. C.

SINCE December, 1941, when the United States entered the present global war, American soldiers have been sent to many parts of the world. Members of our armed forces are now stationed from Greenland's icy mountains to India's coral strand. In these regions, they are exposed to a variety of climates ranging from the extreme cold of the frigid zone to the intense heat of the tropics. They are also exposed to the innumerable infections of these areas, and therefore the Medical Department of the Army must be prepared to fight disease on a global scale. At the present time there is no malady known to man that may not be encountered by American troops, but the most important of all these disease hazards is malaria.

DISTRIBUTION

The present freedom from malaria of the northern United States and the reduced prevalence of the disease in the South have led to a tendency to underestimate the military importance of this serious infection. This is unfortunate, for even in this country, with its extensive facilities for malaria control, about a million persons are infected each year, and the death rates per 100,000 population have varied from 3.5 in 1935 to 0.9 in 1941.

The United States Army has had a long experience with malaria, in both peace and in war, at home and abroad. Never before, however, has it been faced with exposure to the disease in so many different geographic regions, in each of which the epidemiology differs depending on local mosquito vectors and other factors. Therefore, before indicating our experience with malaria and the scope of the present control program, the epidemiology of malaria from the global aspect will be briefly considered.

It has long been known that malaria is one of

the most important diseases of man. Some years ago Manson¹ remarked, "Directly and indirectly it [malaria] is the principal cause of morbidity and death in the tropics and sub-tropics." Osler² referred to malaria as "the greatest single destroyer of the human race." Today, more than four decades after the discovery of the means of its transmission by mosquitoes, malaria remains a major scourge, exceeding all others in reducing the vitality and impeding the industrial development and political progress of the inhabitants of many tropical, subtropical and temperate countries.

The exact world prevalence of malaria is not known. From a study reported by the League of Nations in 1932 it was concluded that in sixty-five countries over 17,000,000 cases were treated in one year. Obviously, only a small proportion of the total number of patients are treated. In India, for example, each year only 8,000,000 to 10,000,000 are treated out of a total of about 100,000,000 patients, and of these from 1,000,000 to 3,000,000 die.

The world distribution of malaria is indicated in Figure 1. According to Strong³ the disease is prevalent between 45° north latitude and 40° south latitude. The indigenous malaria belt extends from 60° N in Europe (Russia and southern Sweden) to 30° S in Africa (Natal), to 40° S in South America (Argentina), and rarely to 20° S in Australia (Queensland).

EPIDEMIOLOGY

The epidemiology of malaria varies greatly in different parts of the world. In the United States, for example, the most important vector of malaria is *Anopheles quadrimaculatus*. This mosquito breeds by preference in the still, fresh water of pools, lakes and swamps. Naturally, the problem of malaria control here is vastly different from that in Trinidad, where one of the important vectors, *A. bellator*, breeds in water-holding air plants that grow high above the ground on the limbs of immortal

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 25, 1943.

†Director, Preventive Medicine Division, Office of the Surgeon General, United States Army.

trees. There are many other important species in the western hemisphere, each of which has its peculiar breeding habits requiring special methods of control.

The chief vector in West Africa is *A. gambiae*, a domestic mosquito that breeds in any kind of standing water, hoofprints, cart tracks, borrow

primarily in pools and is found in such places as drying river beds, overflow pools, borrow pits, hoofprints and cart tracks, and in slowly running irrigation water. This is a plains mosquito that is not found in the hills above an elevation of 3500 feet. It is interesting to note that this mosquito, which caused the great epidemic in Ceylon in

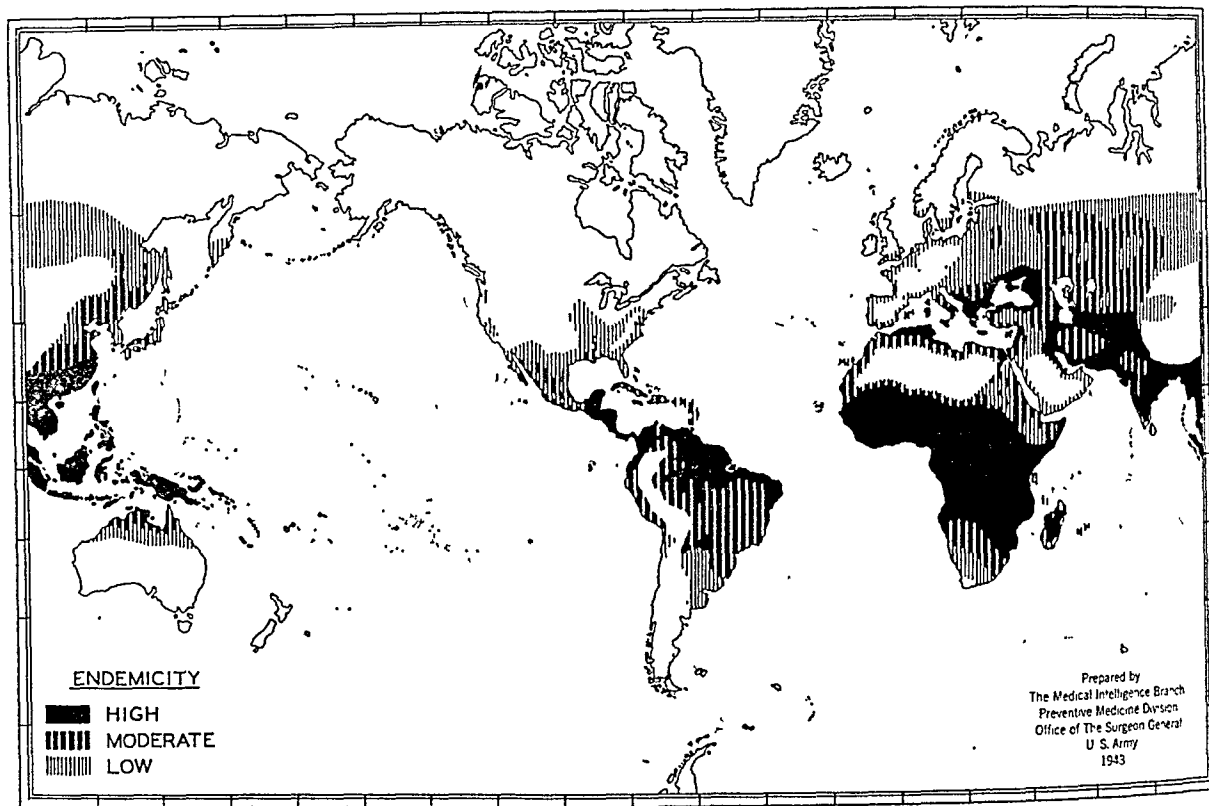


FIGURE 1. Global Distribution of Malaria.

pits, or marshes and even along the edges of slowly moving streams. This is the African mosquito that, in 1930, was transported to Brazil, where it succeeded in colonizing and where, in 1938, it caused the greatest epidemic of malaria ever known in the Western Hemisphere. Fortunately, owing to an energetic campaign by the Brazilian Government in co-operation with the Rockefeller Foundation, *A. gambiae* has apparently been eradicated from Brazil. However, it still remains a great hazard in large areas of Central Africa from the west coast across to the Nile Valley, and even into Eritrea on the Red Sea.

In India there are a number of important malaria vectors with widely different habits. In Bombay, for example, there is *A. stephensi*, a thoroughly domesticated anopheline that, like the yellow-fever mosquito, *Aedes aegypti*, breeds in wells and in standing water in and around houses. Another important vector in India, and the only one in Ceylon, is *A. culicifacies*. This mosquito breeds

1934-1935, is also responsible for the great epidemics that have occurred from time to time in the Punjab of northwestern India.

Another important malaria vector in India is *A. fluviatilis*, which breeds along the edges of foothill streams and irrigation ditches in southern India. It is not normally found at elevations below 1000 or above 5000 feet. A similar mosquito, *A. minimus*, a sunshine and running-water breeder, occurs in central and northeastern India, northern Bengal, Assam, Burma and South China. This stream-breeding mosquito was responsible for a malarial infection rate of 100 per cent in the Chinese troops who escaped from Burma through Assam into India. Undoubtedly, it is as great a hazard to military operations along the Burma border as are the Japanese themselves.

In the Malay Peninsula the principal vector is *A. maculatus*, which breeds by preference in seepage water. There is also a salt-water breeder in southern Malay and throughout the Dutch Indies

that has been undertaken with the advice of the National Research Council and the approval of the Committee on Medical Research of the Office of Scientific Research and Development, office for Emergency Management. (Many separate institutions are making studies, and many thousands of dollars are being spent monthly in the

derogatory to atabrine that are being circulated. The Army is glad that it has adequate supplies of this drug.

The control of malaria in the field depends largely on measures that the soldier can apply for himself. The first of these is the prophylactic use of atabrine or quinine, which should be re-

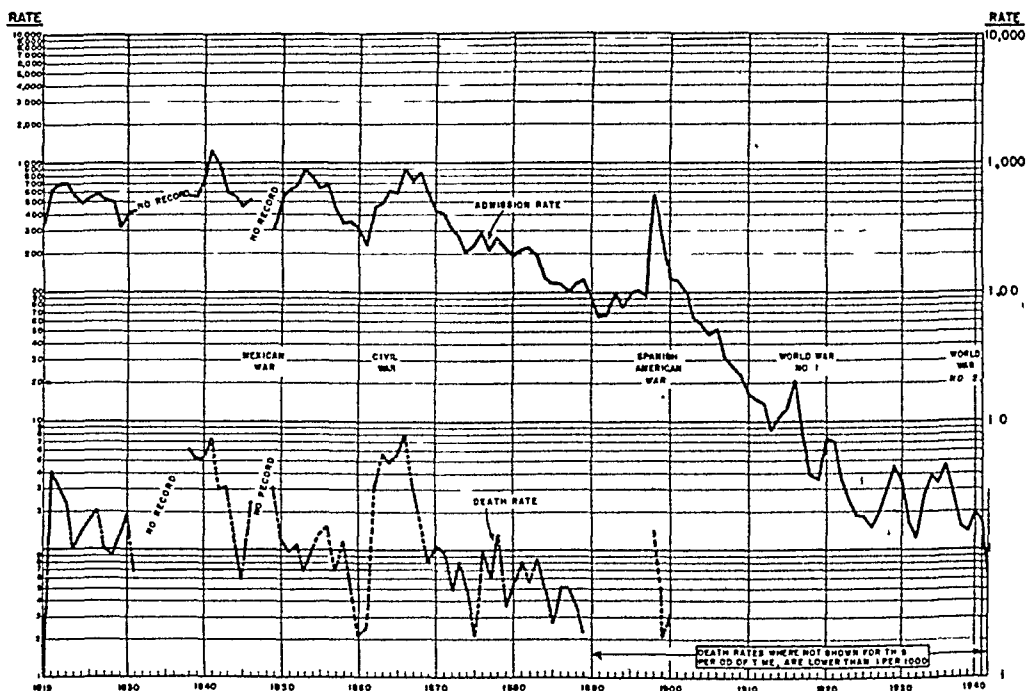


FIGURE 3. Annual Admission and Death Rates (per 1000) for Malaria in White Enlisted Men in the United States Army, 1819-1941.

search for more effective antimalaria drugs; also much valuable research on insecticides and mosquito repellents is being done in close cooperation with the Bureau of Entomology and Plant Quarantine of the United States Department of Agriculture.)

Specific Measures

The malaria-control program includes control measures applicable to permanent camps, posts and stations, and measures that can be used to protect troops living in the field.

The control measures used in permanent installations include all the standard methods employed in civil communities, such as the following: an effective antimosquito campaign, including the elimination of mosquito breeding places by drainage or filling, the destruction of aquatic forms with larvicides and the killing of adult mosquitoes in buildings with insecticide sprays; screening and the use of bed nets in living quarters or other buildings; and the treatment of all infected persons with antimalaria drugs. At this point I wish to warn against the misleading and false rumors

served for emergencies, since neither of them really prevents infection. Both drugs, however, are useful, since they usually prevent the development of clinical symptoms so long as they are taken. This makes it possible for the soldier to stay on his feet and carry out a mission in spite of malarial infection. For at least three years the Army has been concerned with extensive investigations in the search for a more effective malaria prophylactic for use in the field. The second group of measures include the use of bed nets, head nets and mosquito-proof clothing, when indicated and practicable. The third is the use of the new mosquito repellents, which are safe and highly effective. The last measure is the use of freon-pyrethrum aerosol sprays in endemic regions.

Results of the Control Program

The results obtained in the Army's malaria-control program during the recent emergency and present war may be considered in two categories—first, the program in the continental United States, and second, the program abroad.

Control in the United States. At the beginning of the recent mobilization it was feared that the rapid expansion of the Army might cause an increase in malaria among troops in this country. Plans were therefore made early in 1940 to strengthen all facilities for the control of the mosquito vectors in the United States and in our permanent tropical possessions. This program on military reservations has been supplemented by an extra-military program carried on by the United

It has also included the development and procurement of the newly discovered, highly effective mosquito repellents and sprays and of protective nets. Special malaria-survey and malaria-control units staffed by malarialogists, entomologists, parasitologists and sanitary engineers have been sent to our fighting fronts in various parts of the world.

The malarial infection rates in certain overseas regions where protection is difficult are naturally comparatively high and in certain areas they have

TABLE 1. *Annual Admission Rates (per 1000) in Troops in Continental United States and Overseas Theaters, 1942.*

REGION	ALL CAUSES	DISEASE ONLY	INJURIES	RESPIRATORY DISEASE	VENEREAL DISEASE	DYSENTERY AND DIARRHEA	MALARIA
Continental United States	755	664	91	227	38.7	7.15	0.6
Theaters in temperate zones							
A	819	668	152	247	6.8	4.7	—
B	810	664	146	249	3.4	1.7	1.0
C	798	689	109	297	37.0	16.9	—
D	488	408	80	94	9.7	14.9	0.67
Theaters in tropical and subtropical zones							
E	1111	926	185	97	7.7	107.0	47.0
F	1011	833	178	154	33.1	60.1	53.5
G	958	852	106	115	61.0	15.6	106.0
H	1128	1049	79	148	66.0	117.0	173.0
I	1221	1091	130	232	34.0	206.0	38.0

States Public Health Service, working through state and local health departments. As a part of the Army program, sanitary engineers were commissioned and assigned to key positions throughout the Army. An enormous mosquito control campaign was organized and carried out in 1941 at the cost of almost \$2,000,000. During that year the malaria rate not only failed to rise, but actually dropped to an all-time low of 1.7 per 1000. During 1942 the campaign was intensified, and approximately \$3,000,000 were spent. The malaria rate was one third as high as in 1941, namely, 0.6 per 1000. This excellent record cannot be surpassed.

Control overseas. As indicated previously, it is infinitely easier to control malaria among troops living under the stabilized conditions of this country than among those living in the field abroad. By anticipating conditions among our troops overseas, however, it has been possible to set up a control program that is comparatively effective. From the beginning, special facilities have been developed for obtaining information about the incidence and the epidemiology of malaria in all parts of the world. All troops sent abroad have been provided with specific information concerning the disease hazards and the methods of meeting them in the regions concerned. The planning has included provisions for safeguarding, augmenting and distributing the Army's supplies of quinine and atabrine and of various materials for mosquito control.

at times been a matter of some concern. However, on the whole, rates have not been excessive.

In Table 1 are indicated the admission rates for malaria and other diseases in various overseas theaters compared with the rates for similar diseases at home. For obvious reasons the strengths and locations are not shown.

Generally speaking, the health of our troops everywhere has been excellent. The disease rates in all temperate-zone theaters compare favorably with those in the United States, and in some regions they are actually lower than at home. The incidence of malaria is highest in the tropical theaters and among troops in combat areas. It is believed that with the more extensive field use of the new insecticides and repellents the situation even in these areas will improve.

CONCLUSION

In conclusion it is desired to express the appreciation of the Surgeon General of the Army for the whole-hearted way in which the entire medical profession of this country has supported his program for the prevention of all diseases, including malaria. It is also desired to re-emphasize the importance of malaria as a widespread potential hazard to American troops abroad, and to bring to attention the urgent need of more effective methods for its control. I know of no contribution that could be made to American medicine at this time that would be of greater value to this country and to humanity

than the discovery of an easily administered and effective drug for the prevention of malaria among troops in the field. With the support and help of the medical profession, the search for this important drug will continue in the laboratories of our country.

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NEWER CONCEPTS OF GONORRHEA*

SAMUEL N. VOSE, M.D.†

BOSTON

THE remarkable developments that have taken place in every line of endeavor related to the fight against the gonococcus in the last few years have led to a radically altered approach to the management of gonorrhea and a somewhat more optimistic outlook regarding its eventual control. The purpose of this paper is to discuss briefly several phases of this problem, with particular reference to the new opportunities and responsibilities of the practitioner in the light of changing concepts of diagnosis, treatment and prevention.

Gonorrhea, under present conditions, presents a threefold problem. The advent of war has reversed a prior trend and has resulted in a considerable increase in the incidence of this disease, thereby creating a problem of military importance. The public-health aspects of the infection are well recognized. The disease remains, however, as much as ever the personal concern of the patient and his physician. In spite of the activities of the federal and state governments and the magnificent work of various social-service agencies, the ultimate objective of complete eradication of this plague can be attained only through the co-operation of all agencies concerned. With income levels rising, the proportion of civilian patients seeking treatment from the private physician instead of the clinic may well increase. Only if the private physician realizes and accepts his responsibilities and avails himself of the supplementary facilities provided by other agencies will the lot of the patient be improved by such a change. At present, it is perhaps too much to say that the clinic patient receives on the whole better care than the private patient, but certainly the collateral activities such as follow-up and the discovery of contacts are far better organized in the clinic than can ever be possible in private practice. By making use of the supplementary services offered by governmental and other agencies, however, the private doctor can vastly increase his effectiveness in the management of single cases

and his contribution to the solution of the larger problem.

Improvements in methods of diagnosis are principally concerned with the increased reliance on cultural methods to supplement the smear. Formerly considered a difficult and unreliable laboratory procedure, during the last few years culture of the gonococcus has been developed to a point where it is considerably more reliable than is the smear, especially in chronic cases and in the examination of the secretions of the cervix and the prostate gland. Although culture and smear agree in the majority of cases, those in which a positive culture is found with a negative smear outnumber considerably those in which the converse is true. In some cases reliance on clinical observation is the only possible means of diagnosis. A complete history and careful examination may establish a diagnosis even in the face of negative bacteriologic findings, and it must be remembered that in the case of a suspected contact, the male urethra is the best culture medium existent.

Limitations of the use of the culture in private practice are many, and at present perhaps prohibitive for its routine use in all communities. Uniformly reliable results are obtained only in laboratories staffed by technicians having special training and facilities. Mediums must be fresh; the transportation of material for any distance or delay in plating and incubation appreciably reduces the percentage of positive cultures, and overgrowth of other organisms often interferes with satisfactory examination. For following the progress of the average case, the private doctor should depend principally on clinical signs and the stained smear. Where the diagnosis is in doubt, however, or where it is sought to establish proof of a cure, the use of cultures is almost mandatory, even if obtained at considerable inconvenience. The evidence of less than three negative cultures at weekly intervals is not conclusive. Recent experimental work on the transportation of material for culture, notably by Dr. Oscar Cox,¹ of Boston, raises the hope

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†Professor of genitourinary surgery, Boston University School of Medicine; surgeon-in-chief, Genitourinary Department, Massachusetts Memorial Hospitals.

that the availability of this method may be greatly increased in the near future.

Diagnostic measures other than bacteriologic deserve some discussion, especially in the case of so-called "chronic gonorrhea"—a condition that has happily been much less frequent in recent years. Distinction should be drawn between the drug-resistant cases, in which positive smears or cultures indicate the persistence of living organisms, and those in which gonococci cannot be demonstrated in the secretions. In the latter group diagnosis must depend principally on clinical methods, since experience has shown that in only a small proportion of cases is reliance to be placed on the complement-fixation test. Positive results are fairly reliable, but to negative reports little significance can be attached. Clinically, the persistent purulent or crusting discharge at the meatus—the "morning drop"—is almost invariably due to the presence of a large-caliber urethral stricture, a condition that can be detected only by the use of the bulbous bougie—a valuable yet much neglected instrument. Another frequent cause of chronic gonorrhea is infection of the prostate and seminal vesicles, in which case microscopic examination may reveal an excess of leukocytes in the secretion. Following a definite attack of gonorrhea, the finding of pus in the prostatic fluid usually means a persistence of the infection, although it should be borne in mind that a nonspecific prostatitis may have preceded the gonorrheal infection. Urethral stricture and prostatovesiculitis account for the bulk of cases of chronic gonorrhea in males. In females, cervicitis is outstanding as a focus for latent gonorrhea, whether or not it is accompanied by adnexal disease.

The only excuse for mentioning such well-known facts is the frequency with which they are ignored in practice. It has recently been my experience to see a patient who had been treated by bed rest for six weeks on two different occasions on account of persistent urethral discharge. Sulfonamide drugs had brought about disappearance of gonococci, but the discharge had persisted. Massage of the prostate had been carried out on one or two occasions, but no sounds or bougies had been passed. Calibration of the urethra revealed a large-caliber stricture in the anterior urethra, dilation of which brought about the rapid disappearance of the discharge. It goes without saying that no manipulation should be done in the presence of a positive smear.

In a broad sense, a discussion of diagnostic methods may include tests of cure. This is an extremely important matter, and the term "cure" means different things to different people. To the bacteriologist it means the disappearance of organ-

isms from the tissues. To the clinician it should mean not only the elimination of gonococci but the restoration of tissues to a normal condition. To one patient it may mean cessation of the discharge, whereas to another it may signify an unattainable state of bliss that he never hopes to reach. In the latter type of patient the fear of gonorrhea constitutes a disease in itself, and the added assurance afforded by a negative culture is a boon to both patient and physician and well worth almost any inconvenience to secure.

In acute cases that respond quickly and favorably to chemotherapy, the disappearance of discharge and shreds from the urine, together with three or more negative cultures of urethral and prostatic secretions at weekly intervals, may be considered adequate proof of cure. If cultural facilities are not readily available, a much longer period of observation is necessary. Opinion differs concerning the advisability of examining the anterior urethra for stricture in this type of case. As a urologist, I find it difficult to discharge a patient as cured without first assuring myself of the absence of stricture in the anterior urethra, as well as of the normal condition of the prostatic secretion. The passage of a bulbous bougie several weeks after the cessation of symptoms and the disappearance of organisms can do no harm if reasonable care concerning technic is observed and if the disease has been cured. If it has not been cured, the sooner the fact is detected the better.

In chronic cases, the problem is much more difficult. In addition to the disappearance of discharge and shreds and repeated negative cultures, the lapse of several months without recurrence of signs, with the patient under frequent observation, constitutes the best indication of permanent cure. Here again, serologic tests are of limited value, and provocative measures, such as the ingestion of alcohol, are not to be recommended. They are of doubtful value and are not devoid of danger.

With respect to therapy, an excellent pamphlet on gonorrhea issued by the Massachusetts Society for Social Hygiene² in 1936, and circulated for some years thereafter, reads as follows:

The treatment of gonorrhea depends upon keeping all the infected parts that can be reached clean and free from pus, and upon helping the membranes to get well. There is no medicine which will cure it quickly. . . . There is no medicine which, taken by mouth, will cure gonorrhea, or even be of much help.

This was sound doctrine in 1936, as it had been for many years before. The above situation should be compared with that existent at present. The amazing efficacy of chemotherapy has in all but a few cases removed the management of gonorrhea from its status as a urologic procedure into the category

of medical treatment. To such an extent is this true that the urologist, as such, feels some embarrassment in speaking on this subject, except in the way of valedictory. Certainly a disease in which well over 90 per cent of cases are permanently cured by oral ingestion of a drug, and in which suppurative complications have almost disappeared, can call for little action of a surgical nature. That disregard of surgical principles may be disastrous, however, is attested by the occasional patient who appears with the meatus occluded by a wad of cotton under the foreskin and wondering why his infection has failed to respond to the new drug.

The chemotherapy of gonorrhea has received such thorough discussion in the last few years that extended comment is unnecessary. It is generally agreed that most acute cases respond to a dosage of 20 gm. of the chosen drug, distributed over five or more days. If cure does not result from the first course or if cultural proof of cure is not obtainable, a second course of similar dosage should be given. For routine use, sulfathiazole is the drug of choice. Sulfadiazine appears to be equally efficacious, but it is more expensive and its lack of toxicity is largely a theoretical advantage, since serious reactions from sulfathiazole in the dosage mentioned above are rare. Newer drugs at present under trial have little to offer over sulfathiazole. Attention to general hygienic measures and avoidance of alcohol and sexual activity are of course essential. A large fluid intake is desirable. In the average case, rest in bed is not necessary and the patient's occupation need not be interrupted.

Cases resistant to sulfonamide drugs form an interesting group. It is generally considered that cases resistant to one of these drugs show little response to others of the group, and that an increase in dosage is of little value. This is true in general, although exceptions occur. One very resistant case in my experience was treated by the usual methods without effect. A massive dose of sulfapyridine was given over a twenty-four-hour period preliminary to a contemplated fever treatment, and the patient showed such marked improvement that the heat treatment was considered unnecessary and complete recovery ensued without it.

Several courses are open for the treatment of those cases in which response to the routine administration of sulfathiazole is not satisfactory. A shift to another drug of the sulfonamide group and a period of bed rest for ten days or two weeks are the first measures to be tried. Gentle local treatment of the types in common use prior to the advent of the sulfonamide drugs will in a few cases tip the scales in favor of recovery. Fever therapy properly administered produces a cure in a large percentage of cases, but has definite disadvantages.

It requires extensive facilities and constant supervision, and is not without danger to life. Only serious complications or extremely refractory infections justify its use, and then only in otherwise healthy subjects. Results are seemingly better if a preliminary large dose of a sulfonamide drug is given during the preceding twenty-four-hour period. Treatment by various types of vaccines or filtrates has in my experience been extremely disappointing and in some cases serious complications have been attributed to their use. Their field of usefulness is extremely limited.

Other chemotherapeutic agents such as penicillin may be extremely useful in the treatment of sulfonamide-resistant cases. This subject is now under investigation, and *in vitro* tests show that the gonococcus is extremely sensitive to the action of penicillin. According to a recent report,³ penicillin has shown great promise in the treatment of gonococcal infections in man. Further work on this subject will be awaited with interest.

It is in the field of prevention and control that the private practitioner can find the most important of the new opportunities afforded by recent innovations. The establishment of state clinics on a large scale and the large amounts of money spent by the federal government in research on gonorrhea are indicative of the importance of this problem. The value of the work of the social services of large institutions and private agencies such as the Society for Social Hygiene cannot be overrated. As a result of all these activities, the means and organization are now available to bring about the eradication of this disease if properly employed. The above agencies cannot do the job alone, however, and the large number of cases in which the private doctor constitutes the only contact with the patient increases his responsibility.

Measures that help to prevent the spread of gonorrhea include, first, the continuation of treatment until cure is established. A full discussion of the situation on the occasion of the patient's first visit goes a long way toward gaining confidence and preventing a lapse of treatment. A certain proportion of treated cases become asymptomatic carriers, and it is in this group that cultures as tests of cure are of extreme importance. If adequate facilities for culture are not available nearby, the reference of the patient to a laboratory in a large center should if possible be made.

Perhaps one of the most important ways in which the private doctor can co-operate in the prevention of gonorrhea is in reporting lapsed cases and suspicious contacts to his state department of health. In the past such co-operation in regard to the venereal diseases has not been so wholehearted as in the case of other communicable diseases. The splendid report recently published by

Dr. E. B. Howard and others⁴ on the epidemiologic investigation of syphilis and gonorrhea in the Army and Navy in Massachusetts is evidence of the excellent results that can be obtained by well-trained and experienced professional personnel in utilizing information regarding contacts. The Massachusetts Department of Public Health is eager for the co-operation of the private physician and will make the best use of any information that can be furnished.

The general practitioner is occasionally called on for advice concerning prophylaxis. It has always been my opinion that thorough washing with soap and hot water, together with micturition immediately after exposure, will in most cases prevent gonorrhea. The external application of calomel ointment and the injection of 1 per cent Protargol into the anterior urethra give added assurance. Recently a report on the oral use of sulfathiazole as a prophylactic has appeared in the literature.⁵ It appears to be highly effective, reducing the incidence of gonorrhea and chancroid in exposed soldiers to a remarkable extent. In single doses of 5 gm. it is well tolerated. Unfortunately, the ef-

fect of a repetition of this dose at frequent intervals over a long period of time is uncertain as regards both cumulative effects and sensitization, and further experimentation seems necessary before the method can be recommended for wide use.

* * *

In conclusion, it may be stated that recent developments in the management of gonorrhea have placed it in the group of diseases that are both preventable and curable. The private practitioner occupies an important position in any program looking to eventual eradication of gonorrhea.

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SUPRALEVATOR ABSCESS

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SUPRALEVATOR abscess is a rare disease with which few surgeons have had an extensive experience. The fairly numerous papers on the subject have consisted chiefly of brief reports in which there has been little discussion of diagnostic and therapeutic problems and particularly scanty reference to the surgical anatomy involved. A recent case at the Framingham Union Hospital has prompted this review of the subject. The diagnosis of supralevator abscess has not previously been made during the fifty years of the hospital's existence.

Infections occurring about the rectum and anus have been classified as infralevator and supralevator according to their anatomic relation to the pelvic diaphragm. Green¹ has subclassified these infections as follows:

Infralevator infections:

Cutaneous: consisting of folliculitis surrounding the anal margin

Marginal: infection at the anal verge not affecting the sphincters.

Ischio-rectal: infection of the ischio-rectal space usually arising from infections about the crypts of Morgagni.

Supralevator infections:

Superior pelvic-rectal.

Retro-rectal.

Submucous or mural: occurring in the submucosa of the rectal wall.

Infralevator infections are relatively frequent and their surgical treatment is well understood. This paper deals with those infections lying above the level of the pelvic diaphragm. In order to understand the problem of supralevator abscess, a brief review of the relevant anatomy is in order.

ANATOMY AND PATHOLOGY

The well-developed fascial layer covering the iliopsoas muscle in the iliac fossa descends over the brim of the pelvis, at which, at the linea terminalis, it is adherent to the periosteum and below which it becomes known as the endopelvic fascia. Descending on the pelvic surface of the obturator internus muscle for a short distance, this endopelvic fascia undergoes a tendinous condensation or thickening that extends along the entire lateral wall of the pelvis. It is from this area of thickening, the arcus tendineus, that the lateral portion of the levator ani muscles takes origin. These muscles, arising on each side of the pelvis, insert into a median

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raphe. The more anteroposterior or medial fibers, arising from the posterior surface of the pubes, are directed posteriorly along the sides of the prostate or vagina to blend with the longitudinal muscle of the rectum near the anal margin² and

stalks, and along them extend the middle hemorrhoidal vessels.

The pelvic peritoneum covering the front and sides of the rectum extends downward for a variable distance to form the pouch of Douglas. It

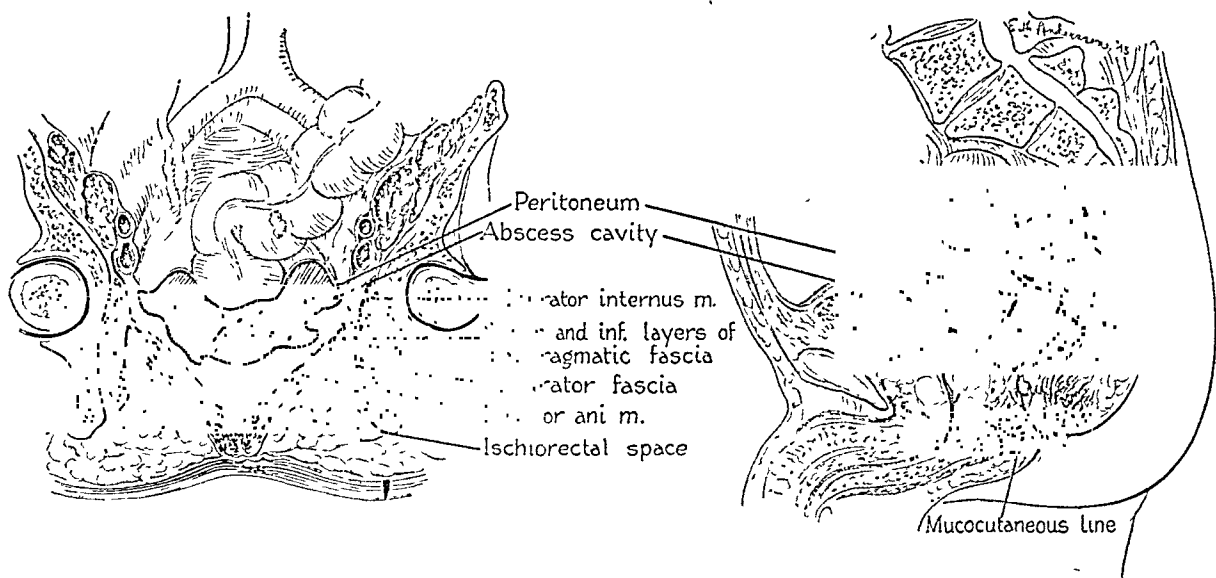


FIGURE 1. Frontal and Median Sections of the Pelvis Showing the Extent of a Superior Pelvirectal Abscess.

Note the extension of the abscess toward the base of the bladder, which frequently results in bladder-neck obstruction.

continue to their insertion on the sacrum and coccyx.

At the arcus tendineus the endopelvic fascia divides into three layers (Fig. 1). The most lateral of these layers descends over the pelvic surface of the obturator internus and pyriformis muscle and is known as the obturator fascia. It forms the lateral wall of the ischiorectal space. The remaining two layers of pelvic fascia are intimately related to the superior and inferior surfaces of the levator ani muscles and are known as the diaphragmatic fascia. The inferior layer of diaphragmatic fascia, also known as the anal fascia, after covering the inferior surface of the levator ani is inserted into the side of the anus and forms the medial wall of the ischio-rectal space. The superior layer of diaphragmatic fascia, also known as the rectovesical fascia, after covering the superior surface of the levator is reflected over the side of the rectum—over the prostate and bladder in the male and over the upper vagina, cervix and bladder in the female. All the pelvic organs in both sexes are thus encased in a fascial sheath that is continuous with the superior layer of the diaphragmatic pelvic fascia.

Lateral fibrous condensations extend from the fascial encasement of the rectum on each side to the lateral portions of the sacrum. These comprise the lateral ligaments of the rectum, or rectal

does not come in contact with the levatores ani but is reflected onto the bladder in the male and onto the cervix and uterus in the female. Between the pelvic peritoneum and the superior surface of the levatores ani there is thus a potential space that contains adipose tissue. It extends from the fascial covering of the prostate or vagina anteriorly to the sacrum posteriorly, and between the superior layer of diaphragmatic fascia on each side. This is the supralelevator space, which is divided transversely by the rectum and rectal stalks into anterior and posterior compartments. The anterior compartment has been designated as the superior pelvirectal space, and the posterior compartment is called the retrorectal or presacral³ space.

The supralelevator space is continuous with the ischio-rectal space through the separations between the levator ani and coccygeus muscles, with the gluteal and obturator regions by way of the sciatic notches and obturator foramina,⁴ respectively, and with the extraperitoneal space of the remainder of the abdomen. Suppuration in the supralelevator space may extend through or around the levatores ani into the ischio-rectal space to point in the skin of the perineum. It may, however, point in the gluteal region or the groin, or extend upward into the retroperitoneal and perirenal spaces. In male patients the inflammatory reaction frequently ex-

tends anteriorly about the structures at the base of the bladder, causing acute urinary retention. In view of the many reported cases in which urinary retention has been a prominent part of the clinical picture, it is surprising that this fact has not received more emphasis.

A considerable difference of opinion exists concerning the route by which infection reaches the supralevator space. A careful study of the reported cases indicates that, in the majority, the route of infection remains undisclosed even in those cases that come to autopsy. A notable exception is the case reported by Meyers⁵ in which a twenty-three-year-old man was gored by a cow, the horn piercing the rectal wall just above the levator ani. An abscess developed in the superior pelvic space, perforated the obturator fascia laterally, extended through the great sciatic notch to the gluteal region, and eventually opened through the skin of the buttock. Cure was effected by preliminary colostomy followed by excision of the sinus.

Most writers agree that infection of the supralevator space is likeliest to occur as a result of infection occurring about the mucocutaneous line in the crypts of Morgagni. Miles³ states that supralevator infections always spread from a septic lesion of the rectum or anus by way of lymphatics that extend laterally from the rectum in relation to the levatores ani, a *modus operandi* that Hibshman⁹ considers of the first importance. Several authors⁶⁻⁸ hold that trauma to the rectum above the level of the insertion of the levatores ani by an ingested foreign body may occasionally be the etiologic agent. In the case presented below, the patient attributed his symptoms to a prune pit swallowed two days before. No evidence of trauma to the rectum was found on repeated proctoscopic examination, and no foreign body was recovered in the contents of the abscess.

Morrissey⁹ states that from 82 to 94 per cent of perianal and ischiorectal infections occur in men, and that in about 75 per cent of these there is a history of a previous gonococcal infection. The resulting low-grade nonspecific infection due to secondary bacterial invaders may flare up, spread from the prostate and seminal vesicles, and cause a vesicointestinal fistula or, "depending on the direction and extent of the inflammatory process, [may] end in ischiorectal, superior pelvic or posterior pelvic abscess and, by lymphatic extension, localized suppuration about the kidney." Morrissey further points out that whereas prostatic infection is usually limited in its spread by the rectovesical fascia (of Denonvilliers), infection perforating the seminal vesicle may escape directly into the superior pelvic space. Morrissey's

theory is supported by Drucek,⁸ Bullock¹⁰ and Ingegno and Spitz,¹¹ yet none of these writers present a case that was proved to result from suppuration arising in the genital apparatus. Morrissey's suggestion is, nevertheless, an interesting one, and the process described is anatomically possible. In the case reported below, an extended effort was made to demonstrate evidence of infection in the prostate and seminal vesicles, but without success.

Although it is true that the majority of cases reported have been in men, many have also been reported in women. In fact, the 5 cases reported by Bacon and Reuther¹² occurred in females. In the fifteen-year period from 1928 to 1942, a total of 82 cases in which a diagnosis of fistula in ano, perianal abscess or ischiorectal abscess was made were treated at the Framingham Union Hospital. Of these, 35 (43 per cent) occurred in females, a figure that certainly does not correspond to that suggested by Morrissey. It has been amply shown by Buie¹³ and others that this type of infection arises in the anal crypts.

Infection in the ischiorectal space may extend upward through the pelvic diaphragm to involve the supralevator region. Thompson and Dunphy¹⁴ have reported 3 such cases.

Other routes of infection of the supralevator spaces have been mentioned as possibilities but rarely if ever reported. These include cases resulting from caries or sepsis of the pelvic bones, from retroperitoneal sepsis arising from perforations in the gastrointestinal tract, particularly from appendicitis and diverticulitis, from infection arising in the female genital apparatus, especially postpartum or post-abortion endometritis, and so forth. Finally, infection may be carried directly to the supralevator space by the blood stream.

CLINICAL PICTURE

The clinical picture of supralevator abscess may be extremely confusing, particularly in the early stages. Usually the infection first manifests itself as a general malaise associated with more or less fever and leukocytosis. After a variable period—a few days to two months in the reported cases—during which constitutional symptoms become slowly or rapidly worse, the patient begins to note pelvic discomfort, frequently described as a swelling in or about the rectum. This discomfort is often temporarily relieved by defecation. Gradually symptoms of low-intestinal obstruction with increasing constipation often associated with intermittent diarrhea supervene. In men the inflammatory reaction frequently extends to, or compresses, the structures about the base of the bladder, causing urinary symptoms of varying severity (Fig. 1). Not infrequently acute urinary

retention is the presenting complaint, and this, associated with fever and leukocytosis, may point strongly to the urinary tract as the seat of the lesion. Eventually the symptoms of a deep-seated abscess with severe, localized pain, chills, fever and extreme leukocytosis present themselves.

The diagnosis is usually established by examination of the rectum by palpation, instrumentation or, preferably, both. In the early stages, tenderness may be elicited on palpation at a point slightly above the anal sphincters, usually limited to one side in a superior pelvirectal abscess and posteriorly in a retrorectal abscess, and possibly associated with some localized injection and edema of the rectal wall. Later, as it becomes well formed, the superior pelvirectal abscess tends to surround more or less completely the front and sides of the rectum, pushing in the walls so that a pronounced narrowing of the rectal ampulla is readily seen and felt, but this narrowing differs from that caused by neoplastic disease in that overlying mucosa is intact. Barium enema x-ray studies may be helpful in demonstrating the narrowing. At this stage the retrorectal abscess may push forward the posterior wall of the rectum and be palpable as a tender swelling extending upward for a variable distance. Extreme pain elicited on firm pressure over the skin between the tip of the coccyx and the anus is said to be an important diagnostic sign.¹⁵ In the later stages an abscess arising in one of the subdivisions of the supralelevator space tends to surround the rectum completely by penetrating the rectal stalks. In late and untreated cases, extension to the gluteal regions, groin and so forth may take place.

Urologic studies have not been frequently reported, even in those cases presenting evidence of obstruction of the bladder neck. Certainly careful palpation of the prostate and seminal vesicles should be done in an attempt to determine whether the infection is arising from these structures. Cystoscopic examination was made in the case presented below with essentially negative findings.

TREATMENT

As with suppuration in all other parts of the body, adequate incision and drainage is the only treatment. With reasonably early diagnosis and surgically adequate drainage, spread of the infection to the less accessible regions of the pelvis and sinus formation may be effectively prevented. Well-directed sulfonamide therapy may be a useful adjunct to adequate surgery in preventing such complications. In cases presenting evidence of low-bowel obstruction or extensive sinus formation, temporary sigmoidostomy may be of definite

value in putting the pelvic colon and rectum at physiologic rest.

The surgical approach to the superior pelvirectal space may be made by a longitudinal or T-shaped incision lateral to the anal sphincter. The fat of the ischioirectal space is traversed by sharp and blunt dissection until the levator ani muscle is identified by palpation. This muscle and its ensheathing fascia are divided in an anteroposterior direction, perpendicular to the direction of its fibers, and the superior pelvirectal space is entered. Transverse division of the levator fibers is evidently harmless and allows for better drainage than if the muscle bundles are merely separated. Should the abscess extend horseshoe-like around the front and side of the rectum, bilateral drainage through both ischioirectal spaces will allow through-and-through irrigation and improved drainage.

Drainage of the retrorectal space may be done by an incision parallel with and slightly lateral to the coccyx and lower sacral segments. The soft tissues are incised until the presacral pelvic fascia is identified. This structure is divided to allow entrance into the retrorectal space.

Hayden¹⁶ reports good results in several cases of superior pelvirectal abscess by instituting drainage through the rectal wall at the lower end of the abscess where it bulges into the rectum. Drainage is facilitated by inserting a 12-mm. rubber tube into the cavity and allowing it to protrude through the anus. Hayden warns against making incisions through both the rectal wall and the ischioirectal space and against incising the rectal wall after the abscess has extended into the ischioirectal space, since, in either case, there is danger of producing a high fistula.

CASE REPORT

A 61-year-old, Russian-born Jew was admitted to the Framingham Union Hospital on April 21, 1942. Ten days before admission, he noted malaise and cramping lower-abdominal pain, which he attributed to having swallowed a prune pit 2 days previously. These symptoms were not severe, and he continued working until the 4th day of his illness, when he began to develop headache, fever and generalized muscular aches and pains. A physician found rales at the bases of both lungs posteriorly and recorded a temperature of 103°F. A tentative diagnosis of pneumonia was made and the patient was given sulfathiazole, without improvement. The following day he noted difficulty in getting the urinary stream started and some burning on urination, and passed only small amounts of urine at a time. There was no incontinence, but the dysuria became progressively worse and this, together with fever, was the chief complaint. Twenty-four hours before admission, he suffered acute urinary retention for which catheterization was required. For the 4 or 5 days immediately preceding admission the bowels did not move in spite of repeated enemas, the abdomen became

moderately distended, and the patient complained of fullness in the rectum. There was no nausea or vomiting.

The past history included typhoid fever at the age of 21, a productive cough for many years, attributed by the patient to cigarette-smoking, and prolapsing hemorrhoids with occasional rectal bleeding for at least 20 years.

Physical examination revealed a poorly nourished man of small stature who appeared to be moderately acutely ill. The temperature was 101°F., the pulse 86, and the respirations 26. An adenoma about 1 cm. in diameter was palpable in the isthmus of the thyroid gland. The chest showed limited but equal excursion on both sides. At the lung bases, particularly the left, were numerous moist rales. The heart was not enlarged and the rhythm was regular, but there was a harsh systolic murmur over the aortic area. The blood pressure was 175/75. The abdomen was slightly distended and peristalsis was hyperactive, but there was no tenderness or other evidence of peritoneal irritation, and no masses could be felt. Rectal examination disclosed a firm, slightly irregular and practically nontender mass extending upward from the level of the upper border of the prostate as far as the examining finger could reach. The rectal mucosa overlying the mass was unbroken, as was demonstrated by repeated proctoscopic examination, and the mass caused a marked constriction of the rectal ampulla. This constriction was largely produced by displacement of the lateral walls of the rectum toward the midline, and to a lesser extent by posterior displacement of the anterior wall. The prostate was small and completely nontender, and the seminal vesicles could not be felt. The prostatic secretion was normal on microscopic examination. The posterior rectal wall did not appear to be involved. There was no tenderness over either ischioanal space. Proctoscopic examination, in addition to demonstrating the constriction, which would not allow the instrument to pass, showed some injection of the rectal mucosa. There was a rosette of internal and external hemorrhoids, but no evidence of recent sepsis or trauma to or around the mucocutaneous line. Cystoscopic examination revealed slight injection of the trigone but no other abnormalities of the bladder or prostate. The ureteral orifices were normal, but the ureters were not catheterized.

The white-cell count was 32,000, with 97 per cent neutrophils. There was no anemia, and blood-chemistry studies were within normal limits. X-ray examination (Fig. 2) demonstrated narrowing of the rectal ampulla, but the remainder of the colon showed no abnormalities. The chest showed evidence of chronic bronchitis. The bones of the lumbar spine and pelvis were within normal limits.

The patient was placed on constant urethral-catheter drainage and was given small doses of sulfathiazole by mouth. On this regimen the temperature and white cell count rapidly approached normal. During the early part of the hospitalization, enemas were productive of gas and feces, and the symptoms of obstruction suffered prior to admission were partially relieved. The palpable portion of the rectal mass remained unchanged, but after several days symptoms of low intestinal obstruction became more acute.

Because the symptoms of low colonic obstruction were associated with some increase in abdominal tenderness, laparotomy was performed on May 2. Exploration of the peritoneal cavity revealed no abnormalities except in the pelvis, where a mass that appeared to be inflammatory

in origin extended upward from the pelvis, surrounding the rectosigmoid and elevating the peritoneum of the pelvic floor. No evidence of diverticulitis was found. There was moderate distention of the entire colon. A long-loop sigmoidostomy was done.

Following the sigmoidostomy, the patient's condition improved. The temperature, pulse and white-cell count returned to normal and the rectal mass began to regress.



FIGURE 2 Barium Enema Showing Narrowing of the Rectal Ampulla.

A urethral catheter is in place.

On the 10th postoperative day, the urethral catheter was removed and the patient was able to void satisfactorily with no residual urine. Because of the striking local and general improvement, further surgery was delayed in the hope that complete regression would take place. By the 14th postoperative day, the mass was much smaller and the constriction of the rectal ampulla allowed the easy passage of two fingers. Thereafter there was no further regression, and on the 17th postoperative day softening of the mass was noted, particularly on the left side. On the following day, the supralevator space was opened by dividing the fibers of the left levator ani muscle, which was approached through the left ischioanal space. About 180 cc. of foul-smelling pus was evacuated from an abscess cavity that extended anteriorly to the opposite side of the rectum, but that did not extend posteriorly because of the rectal stalks, which were easily identified by palpation. The evacuated pus showed no growth on either aerobic or anaerobic culture.

Following drainage of the abscess, the patient did well and was discharged on the 8th postoperative day. At home the abscess was irrigated daily, but on June 21

he was readmitted to the hospital because the sinus tract leading to the abscess cavity had contracted sufficiently to prevent adequate drainage. Lipiodol injection of the abscess cavity at that time showed it to extend horseshoe-like around the front and sides of the rectum (Fig. 3).

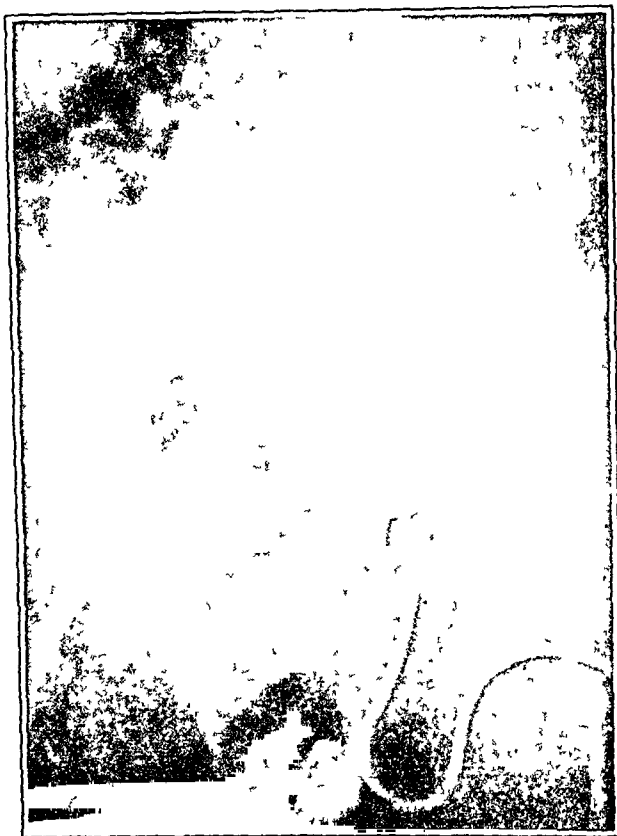


FIGURE 3. *Lipiodol Injection of the Abscess Cavity One Month after the Institution of Drainage.*

More adequate drainage of the abscess was obtained, not only by enlarging the incision previously made on the left side of the anus, but also by making a second incision on the right side, with division of the fibers of the right levator ani muscle. This allowed satisfactory through-and-through irrigation and drainage and, except for a brief interval when a superficial abscess of the abdominal wall required drainage, improvement was progressive and satisfactory. The drainage wounds were kept open until the abscess cavity had closed with granulation tissue, after which the sinuses were allowed to close.

On August 8, the wounds were found to be completely healed. The perirectal mass had completely disappeared, but scar-tissue induration was still readily palpable. On January 4, 1943, 7 months after the abscess had been drained, this induration had completely disappeared and proctoscopic and x-ray studies revealed the rectal ampulla to be normal. The patient was therefore readmitted for closure of the colostomy, which was accomplished without incident. Since then he has enjoyed normal bowel and sphincteric function and has remained well.

DISCUSSION

This case presents several interesting features. The first is that an initial diagnosis of pneumonia

was made. This mistake has been frequently commented on in the literature, and is due to the late appearance of localizing symptoms. The patient had a chronic bronchitis with rales at both bases that were undoubtedly of long standing and were in no way related to the course of the present illness, but that when combined with symptoms of hidden sepsis pointed strongly to the chest as the source of the symptoms.

The second point of interest is the marked local and general improvement that followed sigmoidostomy. As has been stated, this operation was done because of the gradual progression of symptoms and the signs of low-intestinal obstruction. The rapid regression of the mass and the fall of the white-cell count and temperature to normal following the operation gave hope that the products of suppuration would resorb completely without recourse to further surgery. In view of the subsequent course of the disease, it appears that this hope was ill grounded. In cases presenting complicated sinus tracts, sigmoidostomy would undoubtedly prove a valuable preliminary step.

The frequency with which urinary symptoms are present, often as the chief complaint, has been previously commented on and is well illustrated by this case. Cystoscopic examination revealed no intrinsic cause for the obstruction of the bladder neck, which was probably due to extension of the inflammatory process to the structures about the base of the bladder or to pressure on these structures by the mass. Urinary symptoms have not been reported in cases occurring in females.

SUMMARY

The anatomy of the supralelevator space is reviewed, together with a résumé of current theories concerning the routes by which infection takes place. It seems logical to assume that such infection usually arises in the mucocutaneous line and is carried by lymphatic drainage to the supralelevator space.

The clinical picture of supralelevator abscess is essentially one of prolonged sepsis, associated with a perirectal mass and, eventually, with pelvic pain and low-intestinal obstruction. Male patients frequently present symptoms of obstruction of the bladder neck of greater or less severity. The diagnosis is not difficult if the condition is kept in mind.

Treatment consists in early diagnosis followed by adequate surgical drainage. Preliminary sigmoidostomy is occasionally indicated in cases seen late in the disease or in which fistulas are present.

A case successfully treated by surgery is reported.

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THE INTRAVENOUS USE OF LANATOSIDE C*

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IT IS the purpose of this paper to discuss the parenteral use of digitalis glycosides, and to report on the intravenous use of a new glycoside of *Digitalis lanata*, Lanatoside C.

Certain questions regarding the intravenous use of digitalis frequently arise. The physician may ask the following: Is intravenous digitalis therapy necessary? Is it safe? Has it any advantages over other parenteral means of giving digitalis, such as the subcutaneous or intramuscular route? How does Lanatoside C given intravenously compare in action and safety with the other glycosides of digitalis?

It is generally agreed that the average case of cardiac decompensation can be treated effectively by the oral use of digitalis. There are, however, patients with cardiac decompensation with severe symptoms of failure produced both by rapid and irregular and by rapid and regular ventricular action who are often urgently in need of digitalis. Rapidity of action may predominate over all other considerations.

The customary method of full digitalization involves distribution of the drug in such a manner as to produce its full effect within two or three days. The usual method is to give it in divided doses. The average full dose is rarely recommended, for the reason that it is too large for sensitive patients and may result in toxic symptoms. Robinson¹ gave from 15 to 25 cat units of digitalis in a single dose to a series of 26 patients with auricular fibrillation and observed slowing of the heart rate in two to five hours, with the maximum effect in fifteen to twenty-four hours. Although he encountered no reaction in his series, he did not advocate the general use of his method. One and

a half grains of the powdered leaf of digitalis per ten pounds of body weight is a useful working guide, but there is a definite variation in its effect, some patients needing more and some less. It has also been shown that U.S.P. preparations of digitalis when assayed by the frog method vary by as much as 300 per cent.² It can thus be seen that a single dose based on weight carries much uncertainty and danger, even though it may be fairly rapid in action.

Furthermore, many patients with chronic passive congestion have nausea and vomiting and thus must be given digitalis by some other route than the oral one. Levy³ has been an advocate of the rectal route, but according to White⁴ the rectal administration of digitalis, either as a suppository or an enema, is unnecessary and unpleasant. It certainly is not a procedure that invites common usage.

The digitalis glycosides have been administered by the subcutaneous and the intramuscular route. Both are to be condemned. These glycosides when given subcutaneously are intensely irritating; they cause considerable soreness and induration and at times sloughing. Likewise, when given intramuscularly they cause soreness and induration. Clarke⁵ found that a 27 per cent larger dose of digifolin was needed to produce toxic symptoms when given intramuscularly than when given intravenously. Moreover, the reliability of absorption by the former route in cardiac decompensation is highly uncertain. In addition, patients with cardiac decompensation who are unconscious require other methods of administration than the oral one.

Since there is definite indication for the intravenous use of digitalis glycosides it was decided to investigate a new one, Lanatoside C, to determine its rapidity of action and safety when given intravenously.

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travenously, and in the light of these factors, to compare it with other preparations already investigated and in common use. The results are reported below.

In addition to *Digitalis purpurea*, another plant, *D. lanata*, yields digitalis glycosides. In recent years much work has been done on the latter species, and complete chemical elucidation of its products has been accomplished by Smith,⁶ Stoll^{7,8} and other workers.

D. lanata contains three glycosides, known as A, B and C. The A and B components, deprived of one glucose and acetyl radical by enzymatic action, are present in *D. purpurea* in the form of digitoxin and gitoxin. The C component (Lanatoside C) has no chemical relation with the glycosides of *D. purpurea*. Smith has shown that it differs from the genins of other glycosides derived from *D. lanata* and *purpurea* by the structure of its aglucone, digioxigenin. Stoll classified the relation between the two digitalis plants by isolation of all their cardioactive glycosides, together with the products of their enzymatic hydrolysis.

The initial pharmacologic analysis of Lanatoside C was carried out by Rothlin.^{9,10} Its toxicity for the cat and frog was established, and preliminary investigation of its cumulative properties and absorption from the gastrointestinal tract was made. It was found that Lanatoside C is well absorbed and that it has a marked cumulative effect on the heart of the frog and the cat, similar to that of digitoxin. Clinical interest in this substance began with the pharmacologic work of Moe and Visscher¹¹ on heart and lung preparations. Their study suggested that Lanatoside C is the least toxic and the most potent of the *D. lanata* glycosides. Essex, Herrick and Visscher¹² directed their interest toward the problem of the effect of these glycosides on the coronary blood flow and blood pressure of dogs. By inserting a *Thermotromuhr* into the coronary artery, they established that doses of Lanatoside C below the nausea-producing level had no effect on the coronary blood flow of trained dogs. The blood pressure showed no change following intravenous injections of the therapeutic dose.

Lanatoside C is a crystalline substance. Biologic assay is not necessary and its dosage may be determined gravimetrically rather than by the cat-unit method, once its therapeutic efficacy has been established. It is not subject to changes in potency, since it is a chemically pure substance containing no enzymes.

Lanatoside C (Cedilanid) was furnished* for these experiments in ampule form. Each cubic

centimeter of the solution contained 0.2 mg. of the drug. Fahr and La Due¹³ have determined that 8 cc. of the solution intravenously is the optimum digitalizing dose. This was the amount used in the cases reported below.

The slowing of the heart rate in auricular fibrillation as such patients come under the influence of digitalis is a simple and graphic method of observing the onset of the action of digitalis. In order, therefore, to test the efficacy of Lanatoside C, it was decided to study the heart-rate changes in 22 selected cases (Table 1). All these patients had

TABLE 1. *The Slowing of the Apical Rate following the Intravenous Injection of Lanatoside C.*

CASE No.	INITIAL APICAL RATE	SUBSEQUENT APICAL RATE	TIME
			hr.
1	141	78	10
2	144	82	4
3	152	75	3
4	136	71	1/2
5	143	74	2
6	134	71	5
7	154	73	5
8	166	69	3
9	145	72	2
10	144	72	1/4
11	147	73	2
12	138	78	3
13	132	83	6
14	136	82	12
15	164	72	11
16	168	78	4
17	142	84	6
18	164	82	1
19	142	74	3
20	148	78	4
21	134	72	3
22	143	75	5
Average			4 1/3

auricular fibrillation, and none, with one exception, had received digitalis in any form for at least one month. All the patients had original apical rates of at least 120 per minute, determined by stethoscope. Counts were made every five minutes for the first hour and hourly thereafter. The patients remained in bed for at least twelve hours before medication was given in 2 cases in which it was thought that withholding the drug might endanger life. The intravenous route was used in all cases. No other medication was used. Electrocardiograms were made in all cases, to rule out thrombosis of the coronary artery.

The average age of the patients was fifty-four years. There was no classification regarding the severity of decompensation. There were 6 cases of rheumatic heart disease with mitral stenosis and regurgitation, 2 cases of hypertensive heart disease and 14 cases of arteriosclerotic heart disease.

In all cases the heart rate, irrespective of its original level, dropped to 85 or below within twelve hours after receiving Lanatoside C. The average period of fall was three hours and fifty-four seconds. In 2 cases there was a rapid drop, in one

*By the Sandoz Chemical Works, Incorporated, New York City.

from 144 to 72 within fifteen minutes, and in the other from 136 to 71 within thirty minutes. There appeared to be no correlation between the rapidity of drop in the series as a whole and either the original rate or the degree of decompensation.

Figure 1 shows the reactions of apical rate during the first hour at fifteen-minute intervals and each hour thereafter in 4 cases. These are representative of the series. In all the cases there was a drop of 15 to 80 beats within fifteen minutes after

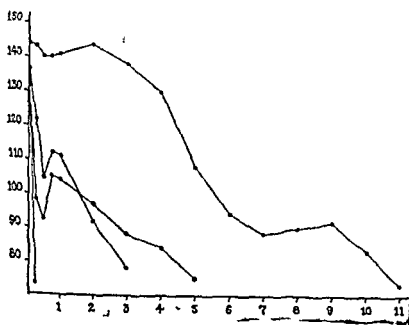


FIGURE 1.

giving the drug, with an average drop of 24 beats. All the patients felt better within half an hour after receiving the medication.

In no case were there any untoward reactions. One patient had been partially digitalized without my knowledge. He received the usual dose, after which he experienced nausea and mild vomiting for two days. Fahr and La Due¹³ gave full digitalizing doses (8 cc.) Lanatoside C intravenously to 4 patients who, unknown to them, had previously been completely digitalized. They developed only transient nausea. Hrenoff¹⁴ and Sokolow and Chamberlain¹⁵ also found no evidence of toxicity when the drug was given intravenously.

For comparison of Lanatoside C with the glycosides of *D. purpurea* regarding rapidity of action and safety following intravenous injection, the study by Pardee¹⁶ offers an acceptable basis. His work included the use of digalin, digifolin and digiton. He found definite slowing of the heart fifteen minutes after the drug was given, with a greater decrease in the next fifteen minutes. From

then on for two or three hours the rate became slightly lower, remaining at that level for twelve to twenty-four hours, with some increase after that time. The dosage was 1 minim per pound of body weight. Pardee advised, however, that the doses be given in fractional amounts rather than in single doses for fear of toxicity. Many of his patients had apical rates of between 90 and 110, which are much lower than any of those in this series. Although there was a fairly rapid drop within thirty minutes in his cases, no rate dropped below 80 in that period. In general, the rapidity of drop was not so marked as that observed with Lanatoside C. This is in accord with the findings of Sokolow and Chamberlain.¹⁵

SUMMARY

Intravenous digitalis therapy may be necessary when rapidity of action is desired and when the patient is unable to take medication by mouth, owing to nausea and vomiting or to unconsciousness. Lanatoside C (Cedilanid) given intravenously has a wide margin of safety, requires no fractional dosage, and is rapid in action. It appears to have a definite advantage over the glycosides of *D. purpurea*.

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MEDICAL PROGRESS

TREATMENT OF SINUSITIS

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THE purpose of this report is to present certain points in the recent literature concerning the treatment of sinusitis that seem sufficiently important to emphasize, without attempting to catalogue all the papers on this subject. In common with a good many other medical problems, the treatment of the diseases of the paranasal sinuses is the object of a good deal of controversy. In an article by Bowers¹ entitled "Practical Points in the Diagnosis and Treatment of Sinusitis" many of these controversial points are mentioned. He notes the lack of agreement among laryngologists and urges that the following points be borne in mind:

Geographic location, since infections act very differently in different parts of the country.

The type of practice (institutional, clinic or private).

The reputation of the author. Is he mightier with the pen than with the scalpel? What is his technic in handling situations? For example, he may state flatly that inflation of the ear is of little value. Does he know how to inflate an ear? If he does, his statement is worth careful consideration; if not, it is worthless. The same thing holds true in all nasal treatment; the skill and dexterity of the operator play a great part in the success or failure of any given procedure.

The author's criterion of success and the measuring rod with which he approaches his work. Definitions vary; what one man calls chronic is not so regarded by another, and ideas as to what constitutes a cure differ widely.

ACUTE SINUSITIS

Practically all authors agree on a conservative approach to the problem of acute sinus infection. In the early stages, rest in bed, applications of heat and the mildest local application possible to obtain drainage are all that is necessary. Henley² advises rest, warmth, vasoconstrictors, vitamin C, chemotherapy, and avoidance of surgery in cases that are not complicated by orbital or intracranial extension. In selected acute cases he uses nasal irrigations consisting of a solution of ephedrine or Neo-synephrine. He also advocates bacterial antigens, foreign proteins and sulfonamide drugs. In cases in which there is inadequate drainage, after giving the above conservative methods a fair trial

he punctures and irrigates the antrum. He is not certain that short-wave and x-ray therapy are of value in the acute congestive stage. In fulminating infection with extension he advocates chemotherapy as an adjunct to surgical drainage. Wishart³ in considering sinusitis in children also advocates conservative treatment unless complications threaten.

As is generally known, the treatment of acute cases has become much more conservative than formerly. Most sinuses subside in the early stages under simple nonsurgical treatment. The treatment of an acute sinus that is not draining presents another problem. If it does not drain, a reaction takes place in the lining membrane and in the surrounding bony wall. The disease passes from the acute to the chronic stage, and so long as acute infection exists there is danger of an orbital complication, osteomyelitis of the frontal bone or extension into the meninges. In the case of an acute nondraining maxillary sinus, a puncture through the lower meatus or irrigation through the natural ostium is indicated. From a study of the anatomy of the natural ostium Bowers¹ concludes that irrigation of the antrum by this route is neither impracticable nor impossible. He thinks that the antrums are retainers of nasal infection and form the keystone to most nasal pathology. In the case of the frontal and ethmoid sinuses the question of technic arises. In general, intranasal operations in acute ethmoiditis and frontal sinusitis are frowned on. Certainly where there is evidence of extension into the orbit the intranasal approach seems illogical. With more familiarity regarding the external approach and a greater knowledge of the cause of failure in frontoethmoidal surgery, much more satisfactory results are being obtained.

There are some exceptions to the above statement. Brown⁴ believes that in children frontal sinusitis calls for intranasal ethmoidectomy, and adds that there should be no interference with the nasofrontal duct. Snow⁵ discusses orbital complications in simple disease, and concludes that early operation and an external approach are necessary.

Boies⁶ brings up again the question of a simple trephining operation for drainage of the frontal sinus in selected cases. These patients suffer from an empyema of the frontal sinus, and drainage under conservative care seems inadequate. Inas-

*The articles in the medical progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas, 1942. \$5 00).

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much as in these cases trauma may cause osteomyelitic complications, it is extremely important to obtain drainage. Boies advocates a simple trephination through the floor of the sinus early in the course of the disease.

CHRONIC SINUSITIS

In chronic sinusitis changes have already taken place in the mucous membrane of the sinus and to some extent in the surrounding bony wall, so that the disease perpetuates itself. The primary factor may be poor nasal drainage during the acute stage or repeated nasal infections that in the course of time have left their mark. Some writers consider other causes, such as dietary disturbances, endocrine imbalance and allergy.

Smith⁷ discusses the management of the nose and the paranasal sinuses in asthma, and advocates treatment by the allergist and the internist before local measures are undertaken. The allergist's study must be thorough to be effective, and requires the co-operation of the rhinologist, especially in children. Smith advises against surgery until the allergy factor is controlled, and even then favors conservative surgery.

Solis-Cohen⁸ discusses the use of specific vaccines in the treatment of chronic sinusitis, but he discourages their use for the prophylactic treatment of acute exacerbations of chronic latent sinusitis, pointing out that severe and harmful reactions may ensue should the organism be the same as that present in the sinus. He first injects intracutaneously in the forearm four test doses. One consists of 0.05 cc. of plain broth, and the other three, 0.05 cc. of the broth culture so diluted that the first contains 1,000,000 to 50,000,000 organisms, the next a tenth to a thousandth of this number, and the last a tenth to a thousandth of the second dose. The smallest amount that gives a slight local reaction is injected therapeutically. Each subsequent dose is regulated in accordance with the general and local reactions produced by the preceding one. A dose is given every five days. Solis-Cohen points out that vaccine therapy may be of no benefit to patients with chronic sinusitis when there is supuration in a sinus that is not draining or when the sinusitis is secondary to an untreated primary focus of infection, such as diseased tonsils.

In considering surgery for chronic sinusitis, the general picture must certainly be considered. An effort should be made to determine whether the sinusitis is the sole disease from which the patient is suffering, or is part of a more complicated picture, such as sinobronchiectasis or sinusitis and bronchial asthma, or focal evidence of infection in other parts of the body.

In an article by Harper,⁹ certain general symptoms are given greater emphasis than heretofore. These are fatigability and mental depression. Fatigability is especially important in aviation medicine. Bullwinkel¹⁰ mentions sinusitis as a cause of fatigue. It has long been known that the average patient with even a moderate degree of chronic sinusitis feels below par and finds it difficult to keep up in his work, which, for an aviator, may be fatal. The same author in discussing nasal accessory sinusitis in aviation medicine states that patients in whom chronic maxillary sinusitis has been treated by the so-called "radical antrum" or Caldwell-Luc operation may be accepted for service, but those who have had a radical frontal or ethmoid operation are dangerous risks. Harper⁹ advocates the Caldwell-Luc operation for chronic maxillary sinusitis, and points out that there is a marked improvement in well-being following this operation, especially in children. In cases of ethmoiditis he approaches the ethmoid sinus through the antrum by the transantral route. In discussing failure in radical surgery, he points out that inefficient treatment is the most frequent cause. Residual bony infection may likewise result in a recurrence of sinusitis. Chronic infection of the sinus alone is comparatively rare. In cases of multiple sinus infection the key to the situation is the ethmoid sinus. This is especially true in frontal sinusitis. In a study of failure in frontal-sinus surgery, I¹¹ found that incomplete ethmoidectomy, as well as failure to remove the frontal-sinus floor completely, was a common cause of reinfection. When one considers the anatomic relations of the ethmoid labyrinth, especially noting the orbital extensions of the ethmoid, the importance of this sinus becomes apparent.

Bowers¹ evaluates certain standard operations. He recommends the Caldwell-Luc operation when there are marked constitutional or tracheobronchial symptoms together with pronounced roentgenographic evidence of disease. The technical steps that he emphasizes are as follows:

- Remove every vestige of membrane.
- Make as large an opening as possible into the inferior meatus.
- If necessary remove a portion of the inferior turbinate to ensure that the opening is not blocked by the turbinate.
- Remove the ethmoid cells through the antrum if they are diseased.
- Pack the opening into the inferior meatus with gauze, but do not pack the antrum.
- Remove the gauze by degrees during the next five days, thus producing some bleeding and thereby adding to the clot in the antrum.

Do not irrigate; use dry agents only in aftertreatment. Dust sulfanilamide powder into the nose and antrum cavity.

At the Massachusetts Eye and Ear Infirmary great care is insisted on to avoid injury to the inferior turbinate, and removal of a portion of it is considered inadvisable. The advantage of a postoperative clot is not clear. Sulfanilamide powder is of great advantage at the time of operation when dusted into the denuded bony cavity. Bowers¹ speaks of the replacement of the mucous membrane lining by a fibrous tissue that may obliterate the antral cavity. Birdsall,¹² in an article discussing the treatment of sinusitis in recruits, points out that postoperatively the antrum shows a thickening due to this formation of fibrous tissue. He cautions that x-ray evidence in operative cases is not a criterion for evaluating the status of the sinusitis in a recruit. The only sign of cure, according to him, is the relief of symptoms.

Patterson¹³ discusses external operation on the nasal sinuses. In considering the surgical approach to the frontal and sphenoid sinuses he emphasizes the importance of the ethmoid labyrinth. The frontal sinus, he states, should always be explored through its inferior wall, the extent of the operation depends on the severity of the disease and the anatomic and pathologic conditions found after the sinus has been opened.

This brings up the question of the type of operation to be performed. There are three classic operations: the Lynch frontal sinus operation, consisting of the removal of the entire floor of the frontal sinus, together with its lining, and complete ethmoidectomy and exploration of the sphenoid sinus if it is involved; the Killian operation, in which the supraorbital bridge is preserved with its periosteum intact; and the obliterative operation, in which the floor, the anterior wall, the entire mucous-membrane lining and often the posterior wall of the frontal sinus are removed.

Patterson¹³ in discussing the obliterative operation advocates the removal of the anterior and inferior wall, together with all the mucous membrane covering the posterior wall. From the experience at the Massachusetts Eye and Ear Infirmary this removal of the mucous membrane is considered essential, since the overlooking of even a small area of mucous membrane inevitably leads to the formation of a mucocele.

Peele and LeJeune¹⁴ mention a direct method for irrigation of the sphenoid sinus by injection with an opaque medium. They discuss the symptoms of sphenoiditis, which are worth mentioning here. In an epidemic of influenza in New Orleans in March, 1940, there was a high incidence of

debility due to sphenoiditis. The symptoms noted among these patients were as follows: headaches radiating from the eyes to the occiput and down the back of the neck and occasionally to the mastoid process; nasal discharge and obstruction; anosmia; aural symptoms due to disturbances of the Eustachian tube by postnatal discharge; blurred vision, photophobia and repeated changes in refraction; retrobulbar neuritis; and changes in mental attitude, believed by the writers to be constant and characteristic in chronic cases, and involving depression, memory defect and irritability. A great many of the patients with mental symptoms were labeled "neurotics," and the diagnosis was occasionally confused with brain tumor. Peele and LeJeune advocate irrigation and, in the cases that cannot be cleared up by this method, operation.

In studying injuries of the frontal and ethmoid sinuses, Calvert and Cairns¹⁵ analyzed 128 cases of traumatic injury to the frontal and ethmoidal sinuses. These cases are interesting from an etiologic standpoint, since they arose from war conditions in Great Britain. Some of the injuries were received in traffic accidents during blackouts, and others were a direct result of bombing. The chief causes are listed as follows: motorcycle accidents (44 per cent), motorcar collisions (19 per cent), being struck by motorcars (9 per cent), bombing, machine-gunning and so forth (8 per cent) and airplane accidents (6 per cent). Seventy per cent of the injuries consisted in compound fracture into the nose or through the skin. In 35 per cent of the series there was anosmia. Twenty-one patients had cerebrospinal rhinorrhea. Of these, 11 were treated conservatively, with 7 recoveries, and 10 were operated on, with 9 recoveries. Nine patients had arocele. Of these, 3 were treated with a dural graft and recovered. Six were treated conservatively, with 4 uncomplicated recoveries. One patient died from meningitis and 1 recovered from it.

In discussing the operative procedure, this author states that if the patient is in good condition, the dural tear should be repaired immediately. If he is in poor condition he should be treated for shock and given chemotherapy and the wound should be cleaned of dirt and debris under local anesthesia. In gross fractures radical removal of the walls of the sinuses should be done. Calvert and Cairns point out, however, that infection of the sinuses was infrequent in these cases.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

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CASE 29411

PRESENTATION OF CASE

First admission. A thirty-four-year-old housewife entered the hospital because of fainting spells and smothering sensations.

Thirteen months before admission the patient caught a cold, which was followed by a persistent cough, wheezing and a smothering sensation in the chest. The wheezing was inconstant and improved considerably after she got rid of her dog; the smothering sensation, however, persisted so that at times she had to rush to the window for fresh air. She developed extreme nervousness and emotional lability. The cough continued, and three months before admission she noticed that she sweat freely, especially at night. There was no fever or hemoptysis, but she had lost 50 pounds in three months.

At the age of thirteen, she bore an illegitimate son, the father being her brother-in-law. A second pregnancy terminated in an abortion. At seventeen she was operated on for "pus tubes." At eighteen she tripped while dancing and fell, injuring her back and fracturing her coccyx, for which she was hospitalized a year. At twenty-two, while unhappily married, she developed attacks of unconsciousness, which had continued to date. The attacks were preceded by a sensation of falling through space; they lasted from two to five minutes and were followed by a "low feeling."

The patient's father died of Miner's asthma and "leaking valve," and her mother of a "stroke."

Physical examination showed a well-developed and well-nourished plump woman lying quietly in bed. The lungs were clear. The heart size was not made out. A short blowing systolic murmur was heard in the third interspace to the left of the sternum. The abdominal and pelvic examinations were essentially normal. The reflexes were hyperactive. The pupils were regular, equal and contracted, even in the dark; they reacted to light and accommodation.

The blood pressure was 138 systolic, 88 diastolic. The pulse was 90, and the temperature and respirations normal.

*On leave of absence

The red-cell count was 4,640,000, with a hemoglobin of 15 gm., and the white-cell count 17,700, with 70 per cent neutrophils. The urine and stools were normal. A blood Hinton test was negative. The cerebrospinal fluid was normal and gave a negative Wassermann reaction. The blood bromide was normal, and all skin scratch tests were negative.

Shortly after finishing the physical examination, following an uneventful trip to the bathroom, she was found unconscious in bed with the eyelids fluttering and the pupils still contracted, although they reacted to light. All attempts to rouse her were unsuccessful. Her pulse and blood pressure were not affected. There were no tonic or clonic movements and no spasticity or changes of reflexes. No effect of carotid pressure on the heart rate could be demonstrated. She gradually regained consciousness, complaining of feeling poorly and of a sensation of falling through space. On the following day she vomited frequently and had two "spells." There were rapid mood changes from hilarity to extreme depression.

A roentgenogram of the chest revealed enlargement of the heart to both sides in the region of the ventricles and auricles. The pulsations were normal. The hilar vessels were surprisingly normal. A gastrointestinal series showed markedly thickened gastric rugae and extensive pyloric spasm but was otherwise normal. An electroencephalogram was within normal limits.

She was placed on Dilantin, 0.1 gm. three times a day, and phenobarbital, ¼ gr. four times a day, following which the attacks stopped. The patient was discharged on the thirteenth hospital day with a diagnosis of epilepsy.

Final admission (thirteen months later). The patient re-entered the hospital because of dyspnea. Her condition had remained about the same but dyspnea had progressively increased, especially after periods of increased activity. Six months before entry she was seen by her physician, who found considerable cardiac enlargement and an enlarged liver. There was no edema. An electrocardiogram revealed normal SR waves. The PR interval was 0.20 second, and the QS interval 0.14 second; the P waves were unusually broad; the QRS complex was slurred in all leads; T₁ and T₂ were inverted; there was evidence of left bundle-branch block. The patient was given digitalis, but owing to signs of toxicity the dose was finally established at 1.5 gr. five times a week. She was placed on a reducing diet and lost 20 pounds in six months. Five months before entry she coughed up slightly blood-streaked sputum, and once a definite presystolic murmur was heard. One month before admission she began to notice abdominal

swelling and pain in the right lower quadrant. Five days before admission she caught "cold" and developed anterior and posterior pleural pain on the right, which subsequently disappeared. There were no chills or fever. For several months she

The temperature was 97°F., the pulse was 80, and the respirations 20.

The white-cell count was 13,200, and the hemoglobin 14.3 gm. The urine showed a + test for albumin and many bacteria. The vital capacity

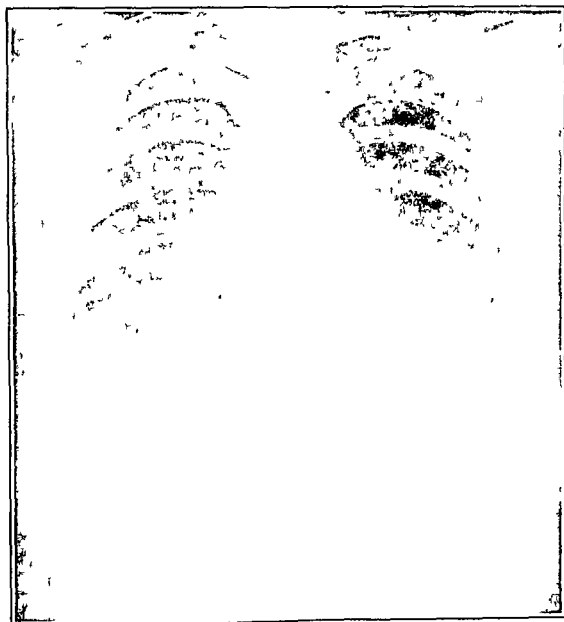


FIGURE 1 *Roentgenogram of Chest.*

felt food stuck in the esophagus at about the level of the third rib.

Physical examination showed essentially the findings recorded at the time of the previous admission, with the following additions. She was dyspneic, even while sitting. The heart was 4 cm. to the right of the midsternal line and 3.5 cm. outside the left midclavicular line. The sounds were of good quality but distant at the apex. The mitral first sound was not snapping, and the pulmonic second sound was greater than the aortic. The lungs were clear except for a few moist inspiratory rales at the right base. The liver dullness extended from the fourth rib to 7.5 cm. below the costal margin in the right anterior axillary line; it was 9 cm. below the right costal margin in the midclavicular line, 10 cm. below the xiphoid, and 11 cm. below the left costal margin.

The blood pressure was 140 systolic, 68 diastolic.

was 1000 cc. (33 per cent of normal). An electrocardiogram showed normal rhythm, with a rate of 80; the QRS complexes in Leads 1, 2 and 3 were wide; T₁ was inverted, and T₂ and T₃ upright. The sedimentation rate was normal. The prothrombin time was 28 seconds (normal, 17 seconds). The hematocrit was 53 per cent. The nonprotein nitrogen was 16 mg. per 100 cc., and the cholesterol 170 mg.

A roentgenogram of the chest revealed marked enlargement of the heart since the first admission (Fig. 1). The enlargement was diffuse. The pulsations were small and rapid. There was enlargement of what was probably the right ventricle. There was a shadow in the left oblique view that could be interpreted as an infarct in the region of the second interspace anteriorly. The diaphragm was low on both sides but showed normal respiratory motion, and there was a small amount of

fluid in the right costophrenic angle. The left main bronchus was elevated. Fluoroscopy was unsatisfactory.

The day after admission, when on the way back from the X-ray Department, she had an attack of unconsciousness similar to those already described. On the evening of the second hospital day, she complained of a sore right shoulder, and on the following morning she began to have pleural pain at the right base anteriorly and posteriorly. She developed a cough productive of bright-red, blood-streaked, mucoid sputum. There was dullness at the right base posteriorly, with suppressed breath sounds and fine rales. Similar rales and a suggestion of a pleural friction rub were heard anteriorly. The lower extremities were not edematous or tender. Fluoroscopy following this attack showed an area of density in the apex of the middle lobe and a small amount of fluid in the right pleural cavity. There were linear areas of density in the left midlung. For the next two days she complained of nausea and vomiting and severe hypogastric pain, which was finally relieved by a copious, light-brown, nonbloody, unformed bowel movement. On the third hospital day she was given 8500 units of heparin intravenously and 300 mg. of dicoumarin by mouth, followed by 10,000 units of heparin and 200 mg. of dicoumarin the next day and 2000 units of heparin the third day. On the same day a blood Hinton test was reported negative but the Wassermann reaction was positive. Two repeated Hinton examinations were positive.

On the fifth hospital day the patient's legs were carefully examined for a possible source of pulmonary emboli. Slight pain was elicited on dorsiflexion of the right foot but no swelling or cyanosis was present. On the following day, during the intravenous injection of heparin, she became unconscious for three minutes, at which time she was completely flaccid and moderately cyanotic without any convulsions. The pulse was slow and strong.

For the next five days she had repeated attacks of pleural pain on one or the other side, with rales and dullness, cough and bloody sputum. The prothrombin time on the eleventh day was 87 seconds (normal, 17 seconds) and the hematocrit was 62 per cent. On the ninth and tenth hospital days she had several attacks of unconsciousness lasting four or five minutes each, similar to those seen previously. The chest pain continued without much change. Bloody sputum and a friction rub were inconstant, but rales and decreased breath sounds persisted over the bases.

On the thirteenth hospital day, eleven days after a menstrual period, she had vaginal bleeding, at

first slight but then profuse. This persisted for three days. On the same day she developed severe pain in the right anterior chest, with cough and bloody sputum. The prothrombin time was 98 seconds (normal, 17 seconds), and the hematocrit 54 per cent. She was placed on potassium iodide, 20 drops daily. During the next twenty-one days she had two other attacks of pain in the left chest, as well as epigastric pain, with cough and bloody sputum. She also had four or five attacks of unconsciousness similar to those previously described. The prothrombin time had decreased to 31 seconds, and the hematocrit was 55 per cent.

During her entire illness the blood pressure remained about 150 systolic, 75 diastolic, the pulse about 90, the respirations 25, and the temperature between 99 and 100°F. The urine usually showed a ++ test for albumin and some red and white cells. She received dicoumarin and heparin almost daily, as well as eight injections of Mercupurin and thirteen doses of digitalis, 1.5 gr., over twenty days.

On the twenty-first hospital day the patient was found dead.

DIFFERENTIAL DIAGNOSIS

DR. EARLE M. CHAPMAN: The first paragraph of the history seems to indicate that the patient had pulmonary disease. Anything that leads to night sweats and a 50-pound weight loss should be considered a rather serious illness. The cough and wheezing that improved by getting rid of her dog make one think that this was an asthmatic episode. I do not know that we should call it asthma, however.

The past history offers tremendous psychiatric possibilities. One could talk on that for the rest of the hour, but I am going to skip over it and say that such events are apt to lead to any complication, especially asthmal. The fainting attacks were not psychiatric manifestations but were quite classic for epilepsy. She had an aura, and then a depressed feeling after the attack.

The patient is described as being plump after losing 50 pounds, so that she must have been obese at one time. I take it that the pupils were small even in the dark. I should like to know the size of the pupils. Of course, Argyll-Robertson pupils are small, being under 2 mm. in diameter.

DR. BENJAMIN CASTLEMAN: They measured 3 mm.

DR. CHAPMAN: They were not small enough for Argyll-Robertson pupils.

I wonder if ineffectual straining at stool had anything to do with the attack of unconsciousness that occurred at the time of the first admission.

I am not aware that people with epilepsy are precipitated into an attack by straining at stool, but the point is raised.

The fact that the pulse and blood pressure were not affected during these attacks is important and leads me to believe that she did not have a carotid-sinus syndrome, Adams-Stokes's disease or some other sort of cardiac arrhythmia that was responsible for the unconscious spells.

After having entertained the suggestion that these attacks were epileptiform, I am surprised to find that the electroencephalogram was normal. This does not help us to establish a diagnosis, but I am sure that one can have epilepsy without a positive electroencephalogram.

The electrocardiogram indicates rather severe myocardial injury and suggests the possibility that this person had had coronary occlusion with myocardial infarction of the anterior wall. One thinks of damage to the myocardium by infection, but there is nothing in the history to indicate this.

The prestolic murmur must be accepted for a fact. It is here in print, and it is an important observation. I presume it was heard at the apex.

I interpret the blood spitting five months before entry as the first sign of pulmonary infarction. The abdominal swelling and pain suggest congestion of the liver, edema and beginning heart failure. The dysphagia is a surprising symptom. There was atypical, generalized enlargement of the heart to both sides. Apparently no murmur was heard later on. The pulmonic second sound was greater than the aortic, which, at thirty-four, is abnormal. The other signs lead one to believe that the patient had congestion in the pulmonary circuit. I assume that there was no aortic regurgitation, since no diastolic murmurs are mentioned and the diastolic pressure was 68.

The elevation of the left main bronchus is a significant observation. On consultation with my friends in the X-ray Department they assured me that the only thing that leads to that is enlargement of the left auricle, which we know was present here. Apparently the right auricle seldom, if ever, leads to elevation of the bronchus. The enlargement of the left auricle fits in with the dysphagia, since impingement on the esophagus would probably lead to difficulty in swallowing at that level.

From the story of the attacks of pain and treatment it seems likely that the patient was suffering from some type of intravascular thrombosis. It does not disclose the source, and we have not enough evidence to say definitely. It is interesting that the first Hinton test was negative and a later one was positive.

"Slight pain was elicited on dorsiflexion of the right foot but no swelling or cyanosis was present." I think they are telling us that the Homans's sign was positive—just a little, possibly, but positive nevertheless.

"For the next five days she had repeated attacks of pleural pain on one or the other side, with rales and dullness, cough and bloody sputum." She apparently was having showers of pulmonary infarcts.

Reconstruction of this case is difficult, to put it mildly. The patient seems to have had epilepsy of twelve years' duration, and under the standard treatment for that disease the attacks cleared up and she was much better. The epileptic attacks seem to have been separate from the other disease, which was chiefly pulmonary. She had asthmatic-like symptoms, with a cough, for thirteen months; then five months before the last entry she had an episode of what sounds like pulmonary infarction, and one month before entry the onset of congestive heart failure. The strange thing is that apparently she developed a positive Hinton test between the two admissions, so that sometime in the thirteen months before the last entry she must have acquired syphilis or one of the reports was a laboratory error. One wonders if changes in the blood serum, owing to some intravascular process, which she obviously had, could have caused a change in the proteins of the blood that would have resulted in this positive reaction. We know that several things cause false positive tests, such as serum sickness and recent vaccination.

As I have said, the problem here is, if possible, to decide what type of heart disease this patient suffered from and what was the mechanism of the failure that led to an afebrile condition with showers of pulmonary infarcts. Against subacute bacterial endocarditis are two facts—the patient had no fever and the hemoglobin was 14 gm. With prolonged endocarditis a fever and significant anemia are almost the rule. The results of blood cultures are not mentioned.

DR. CASTLEMAN: They were not done.

DR. CHAPMAN: It seems that there was a thrombosis in the vascular system, and we have some evidence for believing that it was in the veins, because of the positive Homans's sign.

DR. LAURENCE L. ROBBINS: The films show diffuse enlargement of the heart, but I do not believe that I can help in localizing the type of lesion. The enlarged right ventricle is this shadow on the oblique film. The small shadow in the second interspace is consistent with an infarct. There is relatively little elevation of the left main bronchus.

DR. CHAPMAN: With this evidence it is diffi-

cult to make what would be an easy diagnosis—rheumatic heart disease with mitral stenosis. In support of this we have the following facts: the typical sort of cardiac enlargement, a presystolic murmur, a loud pulmonic second sound and changes in the electrocardiogram that indicate myocardial damage. There is nothing in the history that suggests rheumatic infection, and that makes the diagnosis unlikely to me.

Did she have congenital heart disease, with pulmonary-valve disease, pulmonary stenosis or an interauricular septal defect producing changes in the electrocardiogram? The murmur described was in the third left interspace, and it was the only murmur described while she was in the hospital. Blood cultures should certainly have been taken. There is a possibility that the gonococcus was involved, which frequently attacks the pulmonary valve.

The third thing to consider is coronary heart disease with infarction of the anterior wall which the electrocardiogram indicates. I cannot possibly make this diagnosis on clinical grounds.

The fourth choice is syphilitic heart disease. She had a rather stormy sexual history, with certainly one venereal infection and perhaps another.

This woman must have had a thrombus somewhere in the venous system or in the right heart. I do not believe, however, that she had thrombosis in the veins of the leg. She had no edema, and no symptoms pointing to the pelvic veins or the deep leg veins as being the cause of the emboli to the lungs. So I am going to assume that they arose in the chambers of the right heart, probably the ventricle but possibly the auricle.

Of these four types of heart disease I do not see how one can make a definite diagnosis on the evidence at hand. Syphilis rarely attacks the right side of the heart and certainly there was no sign that the patient had aortic disease or aortic regurgitation, which is the usual pathologic change in syphilitic heart disease. Therefore, I must fall back on some other type, and the commonest of these is rheumatic heart disease. Dr. Robbins told me that elevation of the left main bronchus is seldom, if ever, seen with right-heart enlargement, such as one would have with pulmonary stenosis: Sosman's article¹ establishes this quite clearly. Hence, my final diagnosis is rheumatic heart disease, with mitral stenosis, possibly pulmonary stenosis and certainly thrombosis on the right side of the heart.

DR. CONGER WILLIAMS: The first time we saw the patient on the last admission she had not had a positive Hinton test. Since she had cardiac enlargement without any murmurs and, so as far as

we could tell, without a previous etiologic factor, we considered the possibility of Fiedler's myocarditis,² which gives a picture much like this and sometimes lasts as long as one and a half years. The repeated episodes of pulmonary embolism, which are caused by mural thrombi in the right heart that break off and go to the lung, are consistent with Fiedler's myocarditis. It was possible that she had had syphilis for twenty years. She was first exposed at thirteen. We had no evidence for aortic disease and were never able to hear a diastolic murmur. When the Wassermann test was reported positive, we considered an even more improbable diagnosis,—diffuse syphilitic myocarditis,—and we had to leave it at that and await the autopsy findings.

CLINICAL DIAGNOSES

Fiedler's myocarditis?
Diffuse syphilitic myocarditis?
Multiple pulmonary infarcts

DR. CHAPMAN'S DIAGNOSES

Epilepsy.
Asthma.
Pulmonary infarcts.
Rheumatic heart disease, with mitral stenosis and thrombosis in right side of heart and possibly pulmonary stenosis.

ANATOMICAL DIAGNOSES

Syphilitic aortitis, with involvement of aortic valve and mouths of coronary arteries.
Occlusion of left coronary orifice.
Myocardial fibrosis.
Myocardial infarct, healed.
Cardiac hypertrophy.
Pulmonary infarcts, multiple.
Chronic passive congestion of lungs and liver.
Central necrosis of liver.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The heart was symmetrically enlarged and weighed 610 gm. The entire aorta, but more marked in the ascending aorta and arch, showed the characteristic appearance of syphilitic aortitis. There were raised pearly-gray areas in the intima, such as one sees in the more recent type of syphilitic aortitis, surrounded by the chronic, more usual type of stellate scarring and linear "tree-barking." This was confirmed microscopically by the finding of marked elastic-tissue destruction in the media and lymphocytic infiltration around the vasa vasorum. The mouth of the left coronary artery was completely occluded, and that

of the right markedly constricted. The commissure between two of the cusps showed definite separation, indicating that syphilis had involved the aorta in the sinuses of Valsalva. There must have been some regurgitation, and I cannot understand why a diastolic murmur was not heard. Further evidence that there was regurgitation was the definite flattening of the trabeculae carneae of the left ventricle. There were numerous small grayish-white scars throughout the myocardium, and on the anterior wall a larger healed infarct on which an old organized thrombus was still present. Since the main left coronary ostia was completely occluded, the heart was being supplied by the right coronary artery, which was capacious and had formed a good collateral circulation with the left.

Numerous microscopic sections taken throughout the myocardium showed focal areas of scarring of the type not infrequently seen in a patient with coronary disease. There were no areas of lymphocytic, monocytic or plasma-cell infiltration to suggest a syphilitic myocarditis.

I have to interpret the case as being one of primary syphilitic aortitis with so much involvement of the ostia of the coronary arteries that the resultant anoxia had produced focal scarring of the myocardium. One might possibly think of a burned-out syphilitic myocarditis, but with the ostia of the left coronary completely occluded and the right somewhat narrowed there is sufficient reason for the myocardial fibrosis.

The lungs showed numerous infarcts of various ages. There was no source on the right side of the heart, and I believe that it was in the deep veins of the leg. The liver showed marked central necrosis and evidence of congestive heart failure.

DR. JACOB LERMAN: Was there anything in the brain?

DR. CASTLEMAN: We did not have permission to examine the brain.

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CASE 29412

PRESENTATION OF CASE

A twenty-six-year-old man entered the hospital complaining of pain and stiffness in the back of three months' duration.

The patient stated that he was born with an open spina bifida but that it had closed over. Soon after birth, his mother noted a thin-walled sac over the lumbar region posteriorly. This was treated with alcohol sponges and it shriveled up soon after.

When the patient was fourteen months old, x-ray examination of the lumbar spine and pelvis showed no bony abnormality and there was no positive evidence of spina bifida.

The patient was reasonably well until three months before entry when, while playing golf, he



FIGURE 1. Roentgenogram of Lower Spine.

noticed some stiffness in the midlumbar region. The following day each time he drove a golf ball he felt what he termed a "pull" in the region of the left sacroiliac joint. A constant cramp-like pain was noted in the same region and this continued until admission. Within a week of the onset of this pain he noted that, when rolling over in bed or when suddenly getting up, he felt a sudden "flash of pain" radiating to the left sacroiliac region. An osteopath treated him with prostatic massage and hot enemas; within two or three weeks the flashes of pain disappeared, but the constant pain grew progressively worse. Four weeks before admission, while taken to commu-

y hospital by ambulance, he felt something hard pressing into his back. That evening all the toes of both feet began to feel numb, and within four or five days the numbness had spread to include



FIGURE 2. Roentgenogram of Lumbar Spine following Injection of Lipiodol.

all of both feet. Three weeks before entry he noted that his legs were somewhat shaky and weak, and a few days later he was not able to control his legs as well as he had formerly. At about this time he noted numbness over the knees, and rotating his head or pressing upon something with his feet always led to lumbar discomfort. On two or three occasions during the two weeks before entry, when excited, he became incontinent of urine and once, while laughing, incontinent of feces. His legs gradually became weaker, and he entered the hospital for therapy.

Physical examination showed a well-developed and well-nourished man with an old spina-bifida scar and surrounding hair growth in the midlumbar region. Both legs were markedly weak. There was hypesthesia of both legs, the posterior

aspect of the right thigh, the posterior aspect of the lower half of the left thigh and the medial aspect of each buttock, as well as over the sacrum and lower lumbar region. The left biceps reflex was greater than the right, and the right knee jerk greater than the left; there were bilateral ankle clonus and Babinski signs, more marked on the right. The lower abdominal and cremasteric reflexes were absent.

The temperature, pulse and respirations were normal.

Examination of the urine was negative. The blood showed a white-cell count of 6500, with 69 per cent neutrophils.

X-ray examination of the spine and pelvis showed marked widening of the neural canal throughout the lumbar region (Fig. 1). The intervertebral disk was absent between the second and third lumbar vertebrae, and these two bodies were in contact with one another. There was no actual fusion or deformity of the bodies. An anatomical variation was present at the lumbosacral region — namely, a partially fused vertebra with large transverse processes. Although the canal was greatly widened, there was no erosion of the lateral masses, and no unusual soft-tissue shadow. There was no interference with the natural curves of the spine. Three cubic centimeters of lipiodol introduced into the spinal canal at the twelfth thoracic interspace showed complete obstruction about 1 cm. below the needle, with a cap formation (Fig. 2). No obstruction was met to the cephalad flow of lipiodol up to the seventh thoracic interspace. A blood Hinton test was negative. A lumbar puncture was negative, the total protein being 26 mg. per 100 cc.

An operation was performed on the seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. JOST MICHELSEN: It is obvious that this patient had a space-occupying intraspinal lesion opposite the first lumbar vertebra. The lipiodol injection at the twelfth thoracic interspace showed complete obstruction about 1 cm. below the needle, with a typical cap formation. Two questions remain to be answered. What type of tumor was found at operation? Did it occupy the extradural or intradural space, or both?

We are told that the spinal canal was greatly widened throughout the lumbar region without erosion of the lateral masses. The combination of such bony changes and cord compression has been described as a characteristic syndrome in extradural cysts.¹ These cysts supposedly develop from a congenital diverticulum of the dura mater

or a herniation of arachnoid through a congenital defect in the dura. The fact that this patient had other congenital abnormalities, which I shall discuss later in more detail, is also in favor of an extradural cyst. In only 1 of 10 cases reported so far, however, was the cyst located in the lumbar area; it usually occurred in the midthoracic region, and was more frequent in adolescents than in adults.² Moreover, enlargement of the spinal canal may be found with other extradural tumors as well as with intradural tumors.

The only conclusion that one may draw is that the lesion was of considerable size, since the widening involved all the lumbar vertebrae. Therefore, neurofibroma and meningioma, the commonest intraspinal tumors, can be ruled out. Ependymomas are occasionally very large. They frequently occur in young adults, and the lumbar region is one of their favorite sites. They also produce widening of the spinal canal. One would expect, however, erosion of the dorsal portions of the vertebral bodies with such marked changes of the interpediculate spaces.

Aside from the enlargement of the canal the lumbar spine showed other abnormalities. The intervertebral disk between the second and third lumbar vertebrae was absent. There was sacralization of the fifth lumbar vertebra. Probably both were congenital anatomic variations associated with the spina bifida that was observed at birth.

Concerning the spina bifida, no evidence of a defect in the closure of the vertebral arches was obtained on admission, but there was a scar in the midlumbar region surrounded by a local overgrowth of hair; furthermore, the peculiar neurologic findings could be well explained by traction exerted on the spinal cord as a result of its attachment in the lumbar region.

The neurologic findings were peculiar because a lesion whose upper level is opposite the first lumbar vertebra cannot produce pyramidal symptoms unless the normal relation of the vertebral column and spinal cord is disturbed. In adults the cord ends at the first or second lumbar vertebra. Even if the difference between the knee jerks is discarded, the bilateral ankle clonus indicates involvement of the pyramidal tracts at or above the fourth lumbar segment, which normally lies opposite the eleventh or twelfth thoracic vertebra.

The pyramidal disorder was probably produced by the tumor itself. If it was due to an associated lesion, a myelodysplasia, which is frequently associated with spina bifida, might have to be considered. The other and better alternative is to assume that the lumbar segments were lower than normal.

At an early fetal stage, the spinal cord occupies the entire length of the vertebral canal. Later, the spinal column grows more rapidly than the spinal cord. The latter, firmly attached to the brain, is drawn upward until the final well-known relation of vertebrae and cord is attained. Attachment of the cord in the lumbar region, as a result of malformations there, exerts downward traction, which interferes with the normal adjustment, which, I believe, occurred in this patient. The cord was anchored at the site of the intraspinal malformation.

It is also justifiable to assume, in view of the absence of any other clue in the story, that the cord compression was due to a tumor that belongs in the group of congenital lesions. Its exact nature can hardly be determined on the basis of the available evidence. It was pointed out that the lesion probably was of considerable size. An extradural cyst is still a good possibility. A search in the literature revealed that cysts of congenital origin have also been found intradurally.^{3,4} Both are uncommon. Intraspinal dermoid or epidermoid tumors are also rare in the lumbar region. Lipomas are not infrequently associated with spina bifida, but the whole picture is so puzzling that one may expect something unusual. That is as far as I can go.

CLINICAL DIAGNOSIS

Tumor of cauda equina.

DR. MICHELSEN'S DIAGNOSES

Congenital space-occupying intraspinal lesion (tumor or cyst in the lumbar area).
Downward displacement of cord, with associated myelodysplasia?
Congenital abnormalities of lumbar spine.

ANATOMICAL DIAGNOSIS

Epithelial ependymoma of filum terminale.

PATHOLOGICAL DISCUSSION

DR. CHARLES S. KUBIK: I shall read part of Dr. Mixter's operative note:

There was a definite cleft in the third lumbar vertebra, by fusion of the spinous processes. On exposure of the dura, a mass could be made out, lying at the level of the lower edge of the first lumbar vertebra and the upper edge of the second. An extension of the dura into the cleft in the third lumbar vertebra was freed up, and the dura was opened throughout the extent of the laminectomy. An oval tumor, 3 by 0.5 cm., was found lying within the roots of the cauda equina, as seen through the dura. This tumor seemed to arise from some structure, probably the filum terminale, in the cauda equina. The roots of the cauda equina were matted together down to the level of the

spina bifida occulta—a normal finding in spina bifida occulta. There was adherence of a few posterior roots to the dura at the level of the spina bifida occulta. The mass was carefully dissected out but was ruptured during the later part of the dissection. It contained turbid, brownish fluid, and it seemed to be a cholesteatomatous cyst with some evidence of bleeding within the cyst. So far as I could make out, all the cyst wall was completely removed. The adherent nerve roots were freed from the dura lower down and were allowed to drop back with the rest of the cauda equina.

The tumor measured 2.5 cm. in length and 1.8 cm. in diameter. A large part of it consisted of a cyst, filled with pale-gray, semigelatinous material and lined with columnar and cuboidal epithelium. Some of the cuboidal cells were ciliated and contained a row of granules just beneath the ciliated surface. They resembled cells often found in a persistent central canal of the spinal cord in infants, and indicate that the tumor was an ependymoma.

DR. W. J. MIXTER: The patient made a good convalescence but the left leg was somewhat spastic at the time of discharge. Several weeks later he reentered the hospital following a bout of alcoholic

excess; there were retention of urine, loss of rectal control and weakness and spasticity of the left leg. Examination suggested a large functional element but the spasticity, of course, could not be explained on that basis. A lumbar puncture performed below the level of the operative scar showed no evidence of block. He recovered gradually from this episode and was discharged with full control but still somewhat spastic.

I believe that the spasticity was probably due to some congenital anomaly of the dorsal cord rather than to traction on nerve roots, since no evidence of such traction was seen at the time of operation.

A recent report states that the patient is doing well, but I imagine that examination would still show evidence of spasticity.

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WHEN JOHNNY COMES MARCHING HOME

"NEVER," said Winston Churchill, coining one of his most famous epigrams, "have so many owed so much to so few." He referred, of course, to the defense of England by the Royal Air Force in those desperately heroic days of 1940. The tribute was sincere—it was deserved—and no reward was offered.

We Americans, more mercurial and having suffered so much less, find it necessary to twist our eagle's tail feathers quite frequently, to hear him scream. True, we also have an aggregation of

stout-hearted young men in our services who are rendering excellent accounts of themselves wherever they may be—in the air, on the land, on the restless surface of the ocean and in its waveless depths. They are for the most part modest youths, but by our very idolization of them we are making their eventual return to a civilian status doubly difficult.

It has been the grim duty of occasional generations of youths, in peace-loving countries, to forsake their normal ways of life and to assume the unaccustomed burden of arms, for a time, in defense of the peace that they have always cherished. Their countries owe them a great debt of gratitude for their sacrifices, but they owe them an additional and still greater practical debt—that of helping them eventually to return to useful citizenship so that they may at last enjoy the benefits for which they fought.

The very nature of the hero-worship, for the most part unwelcome and unsought, to which they are subjected tends to unsettle them and unfit them for the necessary readjustment to life on Main Street. As one of our more youthful senators recently remarked to the personnel of a bomber station somewhere in England, "When you come back there'll be nothing too good for you!" We all agree with the enthusiastic young senator, but we wish that his vague promise might have been left unvoiced, and we should like, incidentally, some clear exposition of what we really do owe our men when they return from their complex battle fronts.

The discharge of this debt should certainly assure them peace and security, for that they will have won for everyone, but above all it should extend the opportunity to become rehabilitated as useful, contented, contributing members of a society that they have helped not so much to preserve as to remake, we trust, on a better plane. We do not want them to have a month of adulation followed by a long period of idleness and gradual deterioration punctuated by bonuses, nor do we have the present intention of forcing this year's

fracture. It was high time that an authority made such a selection as has the writer of this textbook—that is, one or two practical and efficient methods that have proved to be safe and generally successful for each of the various types.

After adequately outlining the basic principles of dealing with simple and compound fractures, Dr. Caldwell proceeds to deal specifically with the usual types of fracture, illustrating the methods followed with many line drawings.

The possessor of this volume will be spared a great deal of confusion when he attempts to decide from perusal of present-day literature what is the best method to apply in some puzzling case that has turned up in his practice.

NOTICES

NEW ENGLAND DERMATOLOGICAL SOCIETY

The regular meeting of the New England Dermatological Society will be held in the Skin Out Patient Department of the Massachusetts General Hospital on Wednesday, October 20, at 2 p.m.

SALEM TUMOR CLINIC

A teaching clinic will be held at the Salem Hospital on Friday, October 29, at 9 a.m. The speaker will be Dr. Richard B. Cattell, who will discuss certain aspects of "Carcinoma of the Bowel." A member of the staff will present a survey of some of the hospital cases.

Physicians are cordially invited to attend.

AMERICAN HUMAN SERUM ASSOCIATION

A meeting of the American Human Serum Association will be held at the Children's Hospital, Philadelphia, from 9:30 a.m. to 4:00 p.m. on Friday, October 22, during the war symposium conducted by the American Association of Military Surgeons. A program covering various aspects of shock and its treatment, plasma and blood transfusions, the use of convalescent serums and so forth will be given by authorities in their respective fields. All physicians, particularly those attending the meeting of the American Association of Military Surgeons, will be welcome.

WINTHROP COMMUNITY HOSPITAL

The monthly staff meeting of the Winthrop Community Hospital will be held on Thursday, October 28, at 9 p.m. at the hospital. Dr. William Dameshek will speak on the subject, "Problems of Hematology of Interest to the General Practitioner."

Physicians, nurses and medical students are cordially invited to attend.

BOSTON DISPENSARY

A clinical staff meeting of the Boston Dispensary will be held at the Pratt Hospital Auditorium on Friday, Octo-

ber 29, at 12:30 p.m. Dr. John W. Strieder will speak on the subject, "Modern Aspects of Surgery of the Heart." Luncheon will be served at 12 noon.

All interested persons are cordially invited.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, OCTOBER 21

THURSDAY, OCTOBER 21

*9:00-10:00 a.m. Medical clinic. Dr. S. J. Thinnhauser. Joseph H. Pratt Diagnostic Hospital.

5:00 p.m. Epidemiologic Factors of Rheumatic Fever. Dr. T. Duckett Jones. Seminar on Diseases of Children. Main amphitheater, Children's Hospital, 300 Longwood Avenue, Boston.

*8:00 p.m. New England Pathological Society. Auditorium of the Boston University School of Medicine.

FRIDAY, OCTOBER 22

*9:00-10:00 a.m. Some Observations on Heart Murmurs. Dr. Samuel Levine. Joseph H. Pratt Diagnostic Hospital.

SATURDAY, OCTOBER 23

*10:00-11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

MONDAY, OCTOBER 25

*12:15-1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, OCTOBER 26

*9:00-10:00 a.m. Medical clinic. Dr. S. J. Thinnhauser. Joseph H. Pratt Diagnostic Hospital.

*12:15-1:15 p.m. Clinicorontgenological conference. Peter Bent Brigham Hospital.

2:00-4:00 p.m. Myasthenia gravis clinic. Out Patient Department, Massachusetts General Hospital.

WEDNESDAY, OCTOBER 27

*9:00-10:00 a.m. A Clinical Discussion of Granuloma Inguinale with Differential Diagnosis. Dr. F. M. Thurmon. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

OCTOBER 20. New England Dermatological Society. Notice elsewhere on this page.

OCTOBER 21-23. Association of Military Surgeons of the United States. Page x, issue of September 2.

OCTOBER 22. American Human Serum Association. Notice elsewhere on this page.

OCTOBER 25-30. Postgraduate Courses of the American College of Physicians. Allergy and related topics. Roosevelt Hospital, New York City. Page 570, issue of September 30.

OCTOBER 28. Winthrop Community Hospital. Notice elsewhere on this page.

OCTOBER 29. Salem Tumor Clinic. Notice elsewhere on this page.

OCTOBER 29. Boston Dispensary. Notice elsewhere on this page.

NOVEMBER 8-19. Postgraduate Courses of the American College of Physicians. The course will deal with many aspects of medicine and will be held at various Philadelphia medical institutions. Page 570, issue of September 30.

NOVEMBER 11. Pneumonia as Seen and Treated Today. Dr. Maxwell Finland. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

NOVEMBER 17. New England Oto-Laryngological Society. Page x, issue of October 7.

DISTRICT MEDICAL SOCIETIES

SUFFOLK

OCTOBER 27. Page x, issue of October 7.

DECEMBER 2. Censors' meeting. Page x, issue of September 16.

WORCESTER

NOVEMBER 10. Navy Night. Bancroft Hotel, Worcester.

DECEMBER 8. Worcester City Hospital.

JANUARY 12, 1944. Memorial Hospital, Worcester.

FEBRUARY 9. Worcester State Hospital, Worcester.

MARCH 8. St. Vincent Hospital, Worcester.

APRIL 12. Hahnemann Hospital, Worcester.

MAY 10. Annual Meeting.

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WARTIME RESPONSIBILITIES OF THE UNITED STATES PUBLIC HEALTH SERVICE*

WARREN F. DRAPER, M.D.†

WASHINGTON, D. C.

THE recent trend of events in the war has been encouraging. The fight, however, is still far from won. For years the United States Public Health Service has had its own battle to wage—a battle against death, disease and suffering. Our job is pretty much the same in war or peace. It is heightened, of course, and brought into sharper focus by the exigencies of war; but our function remains always clearly and simply one of maintaining the Nation's health—by "holding the line against preventable disease."

The first eighteen months of war have given the Federal health authorities an opportunity to evaluate their health-protection measures and to clarify those problems most likely to need wartime amplification. The health of the Nation, as measured by death rates and the incidence of communicable diseases, remained good during 1942. Provisional data indicate that the general death rate for 1942 is the lowest ever recorded, 10.3 per 1000 population, as compared to 10.5 for 1941. The increase of fatal accidents in industry almost offset the reduction in deaths from automobile accidents.

One of our functions is the prompt control of epidemic diseases, a threat to the war effort. There have been substantial increases in two epidemic diseases and the outbreak of a new infection among war workers.

Meningococcal meningitis, also known as cerebrospinal fever, caused much loss of life in the last war. In 1942 the incidence of the disease was well above the expected level. This year to date over twice as many cases were reported as for all of last year. The final figures for 1943 will probably show the greatest rise in meningococcal meningitis since 1913. Yet the situation today is much more hopeful than it was twenty-five years ago, when there was no satisfactory treatment. It has

been found, for instance, that prompt administration of sulfonamide drugs will save a great majority of patients and is more effective than the combination of drugs and serum. In some reports to the Public Health Service, the fatality rate has been as low as 5 per cent.

Endemic typhus fever, which increased in 1942, has shown a continuing rise throughout 1943. A year ago an Office of Typhus Fever Control was established with headquarters at Atlanta, Georgia, to assist threatened communities in combating this rise. Surveys of rat harborages are made by this office, buildings are rat-proofed, and rats are destroyed. The Public Health Service also assists the Army in the rodent control of military establishments. In addition, we have been carrying on typhus research for a number of years. One of our officers has developed a vaccine believed to be the most effective of any known for the prevention of typhus. Experiments in the production of live repellents are also encouraging.

Late in 1941, an epidemic eye infection, known as keratoconjunctivitis, appeared in the shipyards of the West Coast and spread through war industries there, and has since attacked numerous industrial groups in other sections of the country. The probable cause of the disease is a virus. It is not a fatal infection, but disables workers for from two to eight weeks and occasionally impairs vision through injury to the cornea. The Public Health Service has widely publicized the conditions among professional workers in state and local governments, the medical field and private industry. Recommendations for the control of this disease have been made. There is, however, no specific cure.

The Public Health Service quarantine authorities are on hand wherever necessary to guard the home front. The great impetus of air traffic—the increased speed of travel—has made it possible for a person to contract any of the quarantinable or

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1943.

†Assistant to the Surgeon General, United States Public Health Service, Washington, D. C.

tropical diseases in distant parts of the world and to reach the United States before the condition has become manifest. Commercial and military aircraft are now examined by medical officers for the presence of disease, passengers are kept under surveillance, and planes are disinfected. Ships touching our ports are inspected for infestation by rats. New ships constructed for the wartime merchant marine incorporate the Public Health Service rat-proofing specifications.

Although reports of infectious diseases from enemy-occupied countries are incomplete, the Public Health Service keeps tabs on the world-wide incidence of disease. We have knowledge of thousands of cases of typhus throughout Europe and Africa. Recent reports show that gastroenteritis, tuberculosis, typhoid fever and trachoma are prevalent in North Africa, and malaria in Morocco and Egypt.

The problem of returning troops infected with various tropical diseases has been studied by the Public Health Service, the Army, the Navy and the National Research Council. These diseases include filariasis, a disease of the lymph nodes for which there is no preventive treatment and no sure cure, and schistosomiasis, also a stubborn long-term disease. The means of transmission in other countries is known, and the Division of Zoölogy of the National Institute of Health is making an extensive study of potential vectors of these two exotic diseases in this country.

At the request of the Navy, a project for controlling the breeding of the mosquito that transmits dengue and yellow fever was instituted at Key West, Florida. Other projects of this type are being undertaken in Texas and South Carolina; they may also be needed at other points along the Atlantic seaboard. The problem of yellow fever has grown more acute as a result of plane travel between this country, West Africa and South America. A vaccine has been produced for this disease. The Public Health Service at the request of the War Department now supplies all the needs of the Army for yellow-fever vaccine to immunize troops.

The control of epidemic diseases, however, constitutes but a small part of the wartime activities of the Public Health Service. Another of our duties is the provision of medical care for merchant seamen and for the entire personnel of the Coast Guard, including the SPARS. Others treated at the marine and contract hospitals are veterans, civil-service personnel injured in line of duty and other legal beneficiaries. These hospital activities have of course been increased by the war. Our program for medical and hospital care of merchant seamen, for example, has been greatly expanded in a co-operative effort with the War Shipping

Administration. Formerly a vast majority of sea-going merchant vessels had no first-aid or sanitation service of any kind. The United States Marine Hospital Corps School in Brooklyn, New York, graduated its first class of two hundred and thirty-nine pharmacist's mates on March 12 after six months of intensive training. This training program and other services—such as the psychiatric treatment of merchant seamen—are joint programs of the Public Health Service and the War Shipping Administration.

At the request of the Secretary of War a number of medical officers, engineers and sanitarians have been assigned to duty with the Army. We have men in each of the ten service commands, at the School for Military Government in Charlottesville and in Panama, Trinidad, Australia, Alaska and North Africa. Several who were on duty in the Philippines have been reported as prisoners of war. Industrial-hygiene experts are serving with the Ordnance Branch of the Army. A number of men have been assigned to duty in different parts of South and Central America in connection with the prevention of the spread of disease from one country to another, and in this country also a group of men are supervising sanitary conditions along the Pan American Highway.

Thousands of Public Health Service personnel are now working in several hundred war areas on assignment to the states, with others assigned to special regional and liaison programs. These are engaged in general public-health work, in industrial-hygiene services, in malaria, typhus, yellow fever and tuberculosis control and in the Civilian Defense plasma-bank programs.

In addition, we offer direct and co-operative services to such war agencies as the Federal Public Housing Authority, the War Production Board, the Federal Works Agency, the Office of Civilian Defense and the War Manpower Commission.

A very important part of our wartime work is assistance in the provision and training of professional personnel. As is generally known, there is an urgent shortage of physicians and dentists in certain critical war areas. Whenever it is impossible to meet the demands for medical care through the Procurement and Assignment Service, the Public Health Service is called on to meet them. Because of the shortage of nurses for the Army, the Navy and essential civilian tasks, we have attempted to increase the supply by stimulating enrollment in schools of nursing and by retraining inactive nurses.

A great portion of our work today is concerned with direct research on wartime problems. Studies now under way for the military authorities include an effort to find a preventive for malaria, the so-

lution of many intricate problems involved in combat flying, improvement in typhus-fever vaccine and other studies that, for military reasons, I cannot describe. Suffice it to say that the military authorities consider these studies of urgent importance.

Research concerning the toxicity and potential dangers of new substances prior to their introduction into industry is constantly going on. These studies are of the utmost industrial importance at this time.

Recently a member of the staff of the National Cancer Institute has succeeded in transforming normal cells grown artificially in the test tube into cancer cells by exposing the cultures to extremely small amounts of a coal-tar chemical that has long been known to induce cancer when injected into experimental animals. The transformed cells when reinjected into animals of the same species from which they were derived have grown rapidly, invading the other tissues of the body and finally killing the animals. It is probable that this contribution will lead ultimately to the discovery of the cause of cancer, since it demonstrates conclusively that the cancer process is started in single cells and is not dependent on constitutional conditions of the whole body. Owing to the increasing recognition of the high incidence of primary cancer of the lung, the National Cancer Institute has made a study of dust collected from a number of industrial cities. It was found, in two successive years, that these dusts contain tar that produces malignant tumors in mice. It is important that these studies be continued. Work is proceeding along the line of developing a chemical treatment for cancer, since the limitations of x-ray and surgery in the treatment for cancer are well recognized. Interesting leads have already been obtained from substances, of bacterial origin. Work is now being done at the Cancer Institute on the development of methods for accelerating the healing of war wounds. Wound healing involves the study of cell growth and proliferation, a field with which research workers in cancer are thoroughly familiar.

A method for relieving the pain of childbirth was developed by two young officers of the Public Health Service at the Marine Hospital in Stapleton, New York, in the past year. Leaders in the medical profession consider this an outstanding contribution. It is an application of the principles of local anesthesia in that it is essentially a process whereby the larger nerves supplying the part of the body involved remain anesthetized throughout the period of painful labor. Mothers remain completely conscious throughout, and, having experienced this relief, are most enthusiastic about the method. The baby being born is not at all af-

fected. Physicians who have witnessed demonstrations have been greatly impressed. The technic is somewhat difficult and requires special ability on the part of the physician. The method is known as continuous caudal analgesia. Possibilities for its use exist in fields of surgery other than obstetrics. The originators have demonstrated their technic at a number of medical schools and are receiving many requests for additional demonstrations.

With the tremendous growth in industry there has been a correspondingly increased need for looking after the health of the workers in the shipyards and munitions plants and for the expansion of health and sanitation activities in all war-industrial areas. For many years we have carried out studies on industrial hygiene. These have now been expanded, field staffs have been organized, and intensive programs to ensure the health of the industrial workers have been instituted. This is done by direct inspections of plants, especially government arsenals, and through forty-four industrial-hygiene units—in thirty-six states, four cities, two counties, the Tennessee Valley Authority and the District of Columbia. The work of state units is so integrated with that of the Public Health Service that a nationwide organization now exists that, if properly implemented, can serve effectively to guard the health of war workers. In connection with the protection of the health of industrial workers, a great deal of work has had to be done in war-industry areas, which grew up nearly overnight in connection with the lack of health and sanitation facilities.

Virtually all Public Health Service research, of course, has been turned to new problems rising from wartime needs. A number of our activities have been in force for a long time, however, although they have been given an additional impetus by the global war. Such are the programs for the control of venereal disease, tuberculosis and malaria.

Mobilization, vast industrial expansion and other conditions of war furnish ideal mediums for the spread of venereal disease. The Public Health Service has co-operated with the military authorities and state and local health organizations in improving conditions in many war-boom communities caught with no defense against venereal infections. The thirty-three hundred venereal disease clinics in the country last year represent a rise of 300 per cent over 1938. Over 10,500,000 treatments for syphilis were given by public-health officers last year, and 64 per cent of the men rejected for military service because of syphilis have already been brought under treatment. Twenty-two rapid-treatment centers for women who are spreading the

disease have been established, and we expect to have sixty more by the end of 1943. Our methods include the new intensive treatments for syphilis and the use of sulfonamide drugs for gonorrhea.

In anticipation of an expected war rise in the incidence of tuberculosis, the Public Health Service strengthened its prevention program by establishing an Office for Tuberculosis Control shortly after the war began. X-ray examinations have been given to nearly 250,000 people, over 160,000 of these being war workers in shipyards, ordnance plants, air depots and other essential war establishments. It is planned to extend the program to include the families of war workers and draft rejectees. All Coast Guard recruits are now examined by this method. We have also been examining Mexican laborers imported into the United States for work in agriculture, mining and railroading. The x-ray examinations are made by

means of a cheap microfilm technic and the use of portable 35-mm. photofluorographic units.

The Public Health Service has had the primary responsibility for the control of malaria in all areas adjacent to naval and military establishments. This work has involved the organization of physicians, engineers, entomologists and other health personnel in a functional and co-operative unit for the basic purpose of eradicating the malaria mosquito. We have protected millions of war workers against the disease. As a result of these activities, too, the Army in 1942 reported the lowest annual malaria rate in its history, 0.6 per 1000 men.

* * *

All this gives a rough idea of what is being done by the United States Public Health Service to maintain the health of the Nation. Much has been and is being accomplished, but much, of course, still remains to be done.

THE EFFECT OF SULFANILAMIDE POWDER ON THE HEALING OF STERILE AND INFECTED WOUNDS*

With Special Reference to Tensile Strength and Ascorbic Acid Content in the Scar

CHESTER M. JONES, M.D.,† MARSHALL K. BARTLETT, M.D.,‡ ANNA E. RYAN, B.A.,§
AND GLADYS D. DRUMMEY, B.S.§

BOSTON

LOW tensile strength of healing wounds in scorbutic guinea pigs was reported by Lanman and Ingalls¹ in 1937 and by Taffel and Harvey² in 1938. In previous communications we³ have demonstrated a direct relation between tensile strength and ascorbic acid content of healing wounds and the ascorbic acid intake in both guinea pigs and human beings.

Further studies of wound healing in guinea pigs maintained at varying levels of vitamin C intake are reported here. The chief object of these experiments has been to determine whether sulfanilamide powder placed in wounds produces any deleterious effect on the healing process. Such a study has seemed particularly timely at the present moment, when the use of this preparation in war wounds has attained such proportions. Although there can be no doubt of the efficacy of a procedure of this kind in controlling wound sepsis, it has seemed pertinent to ascertain whether the indiscriminate use of such a chemotherapeutic agent may interfere in any way with the for-

mation of adequately healed wounds. In addition, we have studied the ascorbic acid content and tensile strength of healing wounds in the presence of induced wound infection or focal infection experimentally produced at a distance from an operative wound, with and without local sulfanilamide therapy and at various levels of ascorbic acid intake.

PROCEDURE

The animals forming the basis of the experiments were divided into three main groups. Group A included guinea pigs of comparable size and age that were maintained on a scorbutic diet throughout the period of study; Group B included animals on the same scorbutic diet with a daily supplement of 1.5 mg. of ascorbic acid; Group C was made up of animals on the same basic diet with a daily supplement of 15 mg. of ascorbic acid. The basic scorbutic diet was that used in previous experiments and originally described by McCullough.⁴ The ascorbic acid supplements were given in aqueous solutions and were administered orally twice a day by medicine dropper. The animals were maintained on these diets for a preliminary

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period of two weeks, previously found to be adequate to establish a tissue level of ascorbic acid.

At the end of this period, an incision of the abdominal wall was made in all the animals, with the following complementary procedures on the basis of a preliminary subgrouping:

Subgroup 1 (control group): No other procedure.

Subgroup 2: Sulfanilamide powder inserted in operative wound.

Subgroup 3: Infection induced distant from operative wound.

Subgroup 4: Infection induced distant from operative wound; sulfanilamide powder inserted in operative wound.

Subgroup 5: Infection induced in operative wound.

Subgroup 6: Infection induced in operative wound and sulfanilamide powder inserted.

The operative procedure was as follows. Under ether anesthesia and surgical asepsis, a midline abdominal incision was made extending from the xiphoid to a point just below the umbilicus. A strip of tissue adjacent to the wound and consisting of the full thickness of the abdominal wall was excised for a control ascorbic acid assay. The peritoneum and muscular layers were closed in a single layer with a running suture of fine silk. The skin was closed in a similar manner in Subgroups 1 and 3. In Subgroups 2 and 4, 0.1 gm. of sulfanilamide powder was sprinkled over the muscle suture before closing the skin. In Subgroups 3 and 4, an infection distant from the operative wound was produced by subcutaneous inoculation with 1 cc. of a broth suspension of a blood-agar culture of beta-hemolytic streptococci. This inoculation was made from three to six hours postoperatively and a walled-off abscess invariably resulted at the site of the inoculation. In Subgroups 5 and 6, the muscle layer was smeared with a ground-up culture of beta-hemolytic streptococci before closing the skin incision, but in the latter group 0.1 gm. of sulfanilamide powder was sprinkled over the streptococcal smear before closing the skin incision.

In each main group the same dietary conditions that had prevailed preoperatively were continued throughout a ten-day period of healing, at the end of which time the animals were killed and the scars were assayed for ascorbic acid content of the tissue and for tensile strength (Table 1). The ascorbic acid content was determined by the method described by Bessey.⁶ The tensile strength was measured by the application of a direct pull

on the healing scar. The apparatus consisted of a 5-cc. glass syringe with collars mounted on the barrel and plunger. Each collar carried a bar pivoted at the center bearing two pins 1 cm. apart. The pivot provided an equalized pull on the tissue mounted on the pins when tension was applied by means of weights placed on the platform. The tissue was mounted on two rather than four pins to allow duplicate determinations on each wound through the use of narrow strips of tissue. As a result of these duplicate determinations, it became evident that there was considerable variation by this method and that only gross differences should be considered as significant. The tensile strength recorded is the weight necessary to rupture the muscle layer rather than the skin layer, as in every case the skin separated first. In scars of high tensile strength the adjacent tissue by which the specimen was mounted tore before the scar itself ruptured. For this reason, figures for tensile strength represent comparative, not absolute, values.

RESULTS

The results obtained in these three groups of animals were as follows:

Group A. As might have been expected from previous studies, the operative wounds in all animals on a scorbutic diet with no ascorbic acid supplement showed little or no evidence of healing. In most cases, although there was some healing of the muscle layer, the skin edges at the site of the abdominal incision fell apart when the sutures were removed. The area of the scar was edematous and inflamed, and in a large percentage of the animals only a scab or a brittle layer of necrotic tissue was formed. Although the muscle layer showed evidence of healing, it required but slight traction to separate the wound. The average tissue ascorbic acid level in this group was very low, regardless of the experimental procedure employed. In the preoperative specimens it averaged 0.32 mg. per 100 gm. of tissue, and in the scars excised after ten days, 0.66 mg. Correspondingly low tensile strengths were noted, the average for the group being the equivalent of a pull of 157 gm. The preoperative values of tissue ascorbic acid in this group corresponded closely to the results reported previously by us³ (0.23 mg. per 100 gm.). Regardless of the additional procedure utilized, no essential difference was noted in any of the animals regarding wound healing, ascorbic acid content of the operative scar or tensile strength. It will be noted that even in this vitamin C-deficient group there was no important deviation from the general average of scar-tissue ascorbic

acid content or of tensile strength in those cases where sulfanilamide powder was introduced into the wound. The lowest figures for tensile strength were those recorded in the animals in which the operative scar had purposely been infected (Subgroups 5 and 6).

Group B. A distinct contrast was observed in the animals maintained on a scorbutic diet plus a supplement of 1.5 mg. of ascorbic acid. As was to be expected, the average ascorbic acid content of the tissue was markedly higher than in the frankly scorbutic guinea pigs of Group A. The average tissue content of ascorbic acid in the preoperative specimens was 0.81 mg. per

and 5.14 mg., respectively. The average figure for tensile strength, 825 gm., was essentially the same as that noted in those receiving a smaller supplement of vitamin C. In one pig (Subgroup 5) with an infected operative wound, a section of the scar that was badly infected and oozing showed a tensile strength of only 125 gm., but the remainder of the wound, which was clean and well healed, resisted a pull of 825 gm.

Although there were occasional wide variations in tissue and scar vitamin C values and in estimations of tensile strength, these were exceptional and in no way altered the trend of the figures obtained

TABLE 1. Ascorbic Acid Content and Tensile Strength of Scars in Guinea Pigs under Varying Conditions of Vitamin C Intake and Varying Experimental Procedures.

GROUP	SUBGROUP	NO. OF ANIMALS	AVERAGE ASCORBIC ACID CONTENT		AVERAGE TENSILE STRENGTH OF SCAR
			PREOPERATIVE TISSUE	SCAR TISSUE	
			mg./100 gm.	mg./100 gm.	gm.
A: Animals on basic scorbutic diet	1: Operation only	7	0.13	1.49	190
	2: Sulfanilamide in wound.....	4	0.00	0.12	260
	3: Distant infection	4	1.05	0.56	180
	4: Distant infection; sulfanilamide in wound....	6	0.01	0.51	170
	5: Infection in wound.....	5	0.39	0.61	80
	6: Infection and sulfanilamide in wound.....	4	0.35	0.71	60
	Averages		0.32	0.66	157
B: Animals on basic scorbutic diet with daily supplement of 1.5 mg. of ascorbic acid	1: Operation only	4	1.19	2.31	670
	2: Sulfanilamide in wound.....	2	0.80	2.24	900
	3: Distant infection.....	5	1.07	2.82	800
	4: Distant infection; sulfanilamide in wound....	3	0.79	2.87	850
	5: Infection in wound.....	4	0.26	2.15	740
	6: Infection and sulfanilamide in wound.....	4	0.77	1.68	1160
	Averages		0.81	2.34	853
C: Animals on basic scorbutic diet with daily supplement of 15 mg. of ascorbic acid	1: Operation only	4	1.92	3.78	740
	2: Sulfanilamide in wound.....	4	2.64	6.25	540
	3: Distant infection	3	1.62	5.02	690
	4: Distant infection; sulfanilamide in wound ...	4	1.14	4.75	640
	5: Infection in wound.....	5	1.04	5.84	780
	6: Infection and sulfanilamide in wound	5	1.00	5.21	1560
	Averages		1.56	5.14	825

100 gm., nearly three times that found in the scorbutic animals. In the ten-day scar the average figure of 2.34 mg. per 100 gm. was obtained, nearly a fourfold increase. The tensile strength of the scar was more than five times greater than that in Group A, the average being 853 gm. In these guinea pigs failure of the scar to heal completely was evident only in animals with induced infection in the operative wounds, and this was observed only in those not treated with sulfanilamide (Subgroup 5).

Group C. The guinea pigs in Group C, in which the diet was supplemented by the daily administration of 15 mg. of ascorbic acid, likewise showed excellent wound healing and, as was to be expected, high ascorbic acid assays of both the preoperative tissue and the scar,—1.56 mg.

in the three main groups. In general, the variations seemed to depend on the nutrition of the animals and on the presence or absence of intercurrent infection. The appearance of the healing wounds in the Group C animals was distinctly better than that noted in those which received a smaller supplementary feeding of vitamin C. In view of a striking increase in ascorbic acid concentration in the scar tissue, the failure to record an increased tensile strength was surprising. Such an apparent discrepancy may be accounted for by the fact that it was rarely possible to measure higher tensile strengths than the average recorded figures because by the method employed the adjacent tissue failed to withstand the additional traction caused by increased weight.

A point of some interest was noted in the scorbutic animals (Group A). In Subgroup 3 distant

infection was produced by experimental abscess formation at a site far from the operative scar. At the end of the ten-day postoperative period it was possible to isolate in the operative scar, which was poorly healed, the same strain of organisms that had originally been used in producing the abscess.

An additional point of interest lies in the apparent effect of vitamin C and sulfanilamide therapy in reducing the mortality in all groups incident to the experimental procedures involving wound infection (Subgroups 5 and 6). During the course of these experiments 30 animals died before the expiration of the ten-day postoperative period. Tissue studies on these animals were not included in the results tabulated in Table 1. Death apparently resulted from infection or infection together with vitamin C lack. In Table 2 are given the mor-

to depend on the general condition of single animals. Occasional discrepancies in the estimations of tensile strength were undoubtedly due to inadequacies in the technical method employed. Nevertheless, the trends in the three main groups were consistent. Failure to obtain maximum increases in the tensile strength of scars commensurate with the increase in ascorbic acid content following high supplements of vitamin C was probably associated with a technical failure to register values above certain levels because of the relative weakness of adjacent tissues. It is highly probable that the greater supplements of vitamin C were associated with the formation of extremely strong scars.

From the results obtained, it is clear that the use of sulfanilamide powder under varying experimental conditions in no way retarded healing or resulted in inefficient scar formation. Further-

TABLE 2. *Mortality Rate in Animals with Infected Wounds.*

CLASSIFICATION	GROUP A			GROUP B			GROUP C		
	NO OF ANIMALS	NO OF DEATHS	MORTALITY %	NO OF ANIMALS	NO OF DEATHS	MORTALITY %	NO OF ANIMALS	NO OF DEATHS	MORTALITY %
Subgroup 5— Wound infection without sulfanilamide	18	13	72	11	10	71	6	1	17
Subgroup 6— Wound infection with sulfanilamide	7	3	43	5	1	20	6	1	17

tality figures as they occurred in the three main groups. Of the scorbutic animals (Group A) with streptococcal infection of the operative wound and no supplement of ascorbic acid, 72 per cent succumbed. Where sulfanilamide powder was placed in the wound, 43 per cent of a smaller group died. Of the animals receiving a daily supplement of 15 mg. of ascorbic acid (Group B), 71 per cent failed to survive when sulfanilamide powder was not used. When the drug was employed, however, only 20 per cent died. Among the animals receiving a maximum daily supplement of 15 mg. of ascorbic acid (Group C), only 17 per cent died. The use of sulfanilamide had no apparent effect on this mortality.

DISCUSSION

Although occasional single determinations of tissue ascorbic acid and tensile strength varied considerably, no important discrepancies were noted. In entire accord with previous results,³ it has been shown that vitamin C lack in guinea pigs is associated with low tissue values for ascorbic acid, poor wound healing, low ascorbic acid values and correspondingly low tensile strength in healing scars. Minor variations in ascorbic acid values appeared

more, the analysis of vitamin C content of postoperative tissue specimens and ten-day scars reveals no evidence that sulfanilamide caused a deviation of ascorbic acid away from scar tissue or increased the need of ascorbic acid in the production of a normal strong cicatrix. In the presence of serious ascorbic acid lack the use of the drug was not effective in promoting better wound healing and a single local dose did not adequately control wound infection. In all three groups of animals there seemed to be one constant factor contributing to poor wound healing. This factor was local infection in the wound. In those animals receiving adequate or massive supplements of ascorbic acid, wound infection was more nearly controlled by sulfanilamide therapy. In the few cases where the infection was not completely controlled, a strong scar was not obtained. An excellent illustration of this fact has already been mentioned in the preceding section. In this case the tensile strength of the uninfected portion of the scar was nearly seven times that of the adjacent portion of the scar, which still showed evidence of sepsis. Obviously, impaired healing was due not to the deleterious action of the drug but to its failure to control completely the local in-

marily an infiltrative, inflammatory process, it may be combined with or replaced by sclerosis, atrophy and scarring of the mucosa. The chief



FIGURE 2. *Klebsiella rhinoscleromatis* in a Space in the Squamous Epithelial Layer ($\times 1400$).
The capsules are stained.

gross features are hard, infiltrated tissues, hard, granular, atrophic mucous membranes that bleed

The disease must be differentiated from several other conditions with which it may be confused. In the early stages, syphilis and lupus may be considered, and the later, more extensive process may suggest cancer or leprosy. The slowly progressive nature of the lesion, usually beginning before the age of forty, a history of origin in the nares or palate and a gradual spread to the entire nasopharynx emphasize the unusual nature of the process. Negative blood Wassermann reactions and failure to respond to antisyphilitic therapy exclude syphilis. Involvement of the lip may suggest keratosis follicularis (White's disease), which, however, is associated with general skin changes. Periarteritis nodosa, in which there are granulomatous lesions in the gastrointestinal tract, may be excluded by the absence of pain locally and in the abdomen. Since those affected frequently care for horses, chronic glanders must be excluded, and this may be done by bacteriologic studies and the Strauss reaction. Ultimately, a biopsy should be performed, which will lead to the correct diagnosis.

Microscopically, the lesion shows characteristic changes the dominant features of which are the inflammatory process and the presence of numerous, large, swollen, vacuolated endothelial cells con-



FIGURE 3. Minute Abscess in the Squamous-Cell Layer ($\times 750$).
It is filled with bacilli and polymorphonuclear leukocytes; none of the organisms are phagocytized.

readily on manipulation and a marked fetid odor. Frequently cancer or tuberculosis is the initial clinical diagnosis, because of the prolonged course of the disease.

taining encapsulated bacilli. These cells were first described by Mikulicz¹⁰ in 1876, and the organism believed to be the cause of the infection was isolated by Frisch¹¹ in 1882. This bacterium is al-

most identical with Friedländer's bacillus (*Klebsiella pneumoniae*).

CASE REPORT

A 66-year-old man, born in Poland, had been a resident of Berkshire County, Massachusetts, for many years. During most of that time he had worked intermittently as a laborer and lived in the country under simple hygienic conditions. He was seen for the first time by a physician in September, 1928, when he visited Dr. F. S. Gospodarek of Adams, Massachusetts, complaining of a mouth condition that he stated had been present at least five years



FIGURE 4. Endothelial Leukocytes in the Epidermis ($\times 1600$).

One contains bacilli with well-developed capsules; the other, bacilli without capsules.

and that had begun to interfere with eating and swallowing. He was certain that the trouble began after a tooth extraction. The mouth was tender but not painful. He had not lost weight and recalled no gastrointestinal symptoms. No other member of the family, which included four children, showed evidence of similar changes in the mouth or nose.

Examination showed a dusky-red, thickened, granular, indurated lesion involving the hard and soft palate. In addition to small and large granulations on the surface there were many deep grooves mingled with grayish areas, apparently cicatrices. The uvula was absent. The process involved the postpharyngeal wall as far as one could see, and also the gum margin of the upper jaw on the left side. On palpation the palate and contiguous buccal mucosa were exceedingly hard, suggesting a scirrhous carcinoma. Manipulation resulted in free bleeding from the surfaces. The nose and upper lip were apparently not involved, but a discharge was present in the nostrils, as well as a foul, fetid odor.

Sections of a small fragment of tissue from the hard palate showed an inflammatory lesion characterized by the presence in the epithelium and subepithelial tissue of large, pale, rounded cells of endothelial type, each containing clear, foamy cytoplasm and as many as forty

somewhat regularly distributed minute rods lying in clear spaces (Figs. 1-5). In some cells the organisms possessed well-defined capsules; in fields where the capsules were absent there were numerous polymorphonuclear leukocytes. The nuclei were small, round and pyknotic and placed in the centers or peripheries of the cells.

Cultures of the nose and palate on a variety of mediums yielded mixed growths in which large, clear, colorless mucoid colonies were a prominent feature. They developed best on human blood agar and attained a diameter of 10 mm. The organisms were short, plump, nonmotile, gram-negative rods with rounded ends, and varied in size from 2 to 8 microns, depending on the growth period. The bacterium was very aerobic, growing best on or near the surface and forming in broth a thick pellicle. Gelatin and Loeffler's serum were not liquefied. Litmus milk was faintly and slowly acidified, and in the various carbohydrate mediums, except lactose, there was acid production but no gas. The organism did not develop on highly acid mediums. Indole was not produced. Cultures were odorless, and the organism resisted drying for 2 weeks.

The patient was next seen in October, 1939. He was then a short and emaciated man and weighed only 90 pounds. Because of increasing difficulty in breathing, a tracheotomy had been performed several months previously. The breath from the tracheal tube was extremely



FIGURE 5. Endothelial Leukocytes Filled with Bacilli of Rhinoscleroma ($\times 1100$).

fetid. The voice was fairly audible. There were no external signs of the disease about the nose or lips.

Examination of the mouth disclosed a greatly contracted oral cavity. The deformed, thickened, granular, scarred palate was drawn down toward the base of the tongue, reducing the oral cavity to about a fourth of its normal volume. The process involved the buccal mucosa, particularly on the left side, to which the base of the tongue was adherent. The tonsils were not visible. The tongue was soft and coated. The anterior gum margins were not involved by the process. Slight rubbing of the palate surfaces resulted in free bleeding. The nasal mucosa was markedly congested but did not resemble the oral membrane. During the preceding 12 years the patient had received only local treatment. As he was living on a remote farm and was somewhat indifferent to medical advice, therapeutic procedures were not adhered to.

A second biopsy was performed in October, 1939, and

sections showed the same type of pathologic change described above. The endothelial cells containing Frisch bacilli were much more abundant than previously. Numerous colonies of the same organism were obtained on plain agar slants from the mouth but fewer colonies from the nose. Cultures made from the fingers by impressing them on agar plates also yielded a few of the same type of colony, and swabbings from the rectum yielded an abundant growth of colonies identical with those obtained from the mouth. Thus, an organism of the Friedländer type was isolated from the nose, mouth, fingers and rectum that was identical with the bacillus isolated 11 years previously.

The patient died in March, 1942, about 20 years after the onset of the disease. The lesion had become slightly more extensive, the fetid odor was more pronounced, and the patient could not breathe without a tracheotomy tube but swallowed liquids well. The terminal symptoms indicated failing heart action. Permission for autopsy was not obtained.

The organism was apparently a member of the coliaerogenes group. It was cultivated in broth and as much as 2 cc. of 18-hour broth cultures was injected subcutaneously and intraperitoneally into guinea pigs and intraperitoneally and intravenously into rabbits, but symptoms were not induced. Subcultured over a period of 14 years the organism still retains its original characteristics and resembles members of the genus *Klebsiella*.

The bacterium corresponds closely with *K. rhinoscleromatis*, described in 1882 by Frisch.¹¹ He believed it to be the cause of scleroma and by injections into the nasal septum of rats was able to produce small tumors. Many other workers have

been unable to develop lesions in ordinary laboratory animals with injections of this organism, and its etiologic role is still uncertain.

* * *

In this case report the points deserving special attention are the specific pathologic changes of the disease, the presence of capsulated gram-negative bacilli in the large endothelial cells and the constant presence in ordinary cultures of *Klebsiella rhinoscleromatis*.

I am indebted to the late Dr. Frank B. Mallory for assistance in the diagnosis and for the photomicrographs.

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CLINICAL NOTE

PROLONGED URETERAL OBSTRUCTION WITH RECOVERY FOLLOWING ADMINISTRATION OF SULFADIAZINE AND SULFATHIAZOLE*

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RENAL complications following the use of sulfapyridine,^{1,2} sulfathiazole^{3,4} and sulfadiazine⁵⁻⁷ may be of serious consequence, with death in some cases rapidly following the development of anuria and uremia. On the other hand, sulfan-

Prolonged toxic reactions following the administration of sulfanilamide and its derivatives are unusual. Review of the literature fails to reveal reports of persistent urinary findings after the sulfonamide has been stopped. The normal pattern of toxicity is manifested by its appearance during administration and its prompt relief on discontinuance. The case reported below is uncommon in that ureteral obstruction persisted for more than two months after discontinuance of the sulfonamide and was completely relieved by ureteral catheterization and irrigation.

CASE REPORT

A. L., a 27-year-old soldier, was admitted to the Medical Service of the Lovell General Hospital on June 11, 1942, complaining of generalized malaise and fever with some aching of the legs and arms of 1 week's duration. On June 9, there had been an attack of vomiting, which was attributed to overeating. The day before admission he felt feverish and the temperature was 101°F. Physical examination was entirely normal, and the patient denied having venereal disease. He had previously been observed



FIGURE 1. Dilatation of the Left Upper Ureter, Kidney Pelvis and Calyces Due to Obstruction of Ureter by Sulfonamide Crystals.



FIGURE 2. Normal Ureter and Kidney Pelvis after Obstruction of the Left Ureter Was Relieved by Catheterization and Irrigation.

ilamide is much less likely to injure the kidney seriously.⁴ According to Keefer,⁸ "it is rare indeed for a patient who has shown signs of renal insufficiency during sulfonamide therapy to continue to show them following the termination of treatment." Most authors agree on the treatment of acute manifestations of renal complications; namely, discontinuance of the drug, forcing of fluids and ureteral catheterization and irrigation when oliguria persists or anuria develops.

at this station in May, for German measles and after 1 week's stay was discharged apparently fully recovered.

Examination showed a well-developed and well-nourished man who appeared ill but not seriously so. The temperature was 99.8°F., the pulse 88, and the blood

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pressure 130/90. The only abnormal physical finding was mild circumorbital edema.

The initial urinalysis revealed a moderate amount of albumin. Microscopic examination of the sediment showed abundant white cells with frequent clumping, an occasional pus cast and 5 to 7 red cells per high-power field. A Kahn test was negative. The sedimentation rate was markedly increased. The white-cell count was 13,000, with 63 per cent polymorphonuclear neutrophils, 7 per cent stab forms, 4 per cent eosinophils, 23 per cent lymphocytes and 3 per cent monocytes. The red-cell count was 4,400,000, with 100 per cent hemoglobin. The blood nonprotein nitrogen was 43.5 mg. per 100 cc. Daily urinalyses revealed persistent albuminuria, pyuria and hematuria.

With these findings in mind, the patient was questioned further and gave the following history. On May 15, after sexual relations 3 days previously, he noted a thin, watery urethral discharge associated with burning, itching and frequency of urination. He consulted a civilian physician, who prescribed sulfadiazine, of which he took 44 gm. over a period of 10 days. At the completion of this course of therapy, the discharge persisted and there was pain in the left upper quadrant of the abdomen associated with the passage of yellowish brown urine. After all medication had been discontinued for 10 days, sulfathiazole was prescribed and 12 gm. was given in 2 days. Ten days later malaise and fever were noted and were the chief complaints on admission.

It seemed likely that the patient was suffering from sulfonamide lithiasis. Accordingly, fluids were forced, the urine being observed closely in an effort to clear the genitourinary tract. In spite of adequate fluid intake and output, the abnormal urinary findings continued. A scout film of the abdomen showed no signs of calculus. On July 13, intravenous and retrograde pyelograms revealed poor function of the left kidney with considerable dilatation and blunting of pelvis and calyces. The lower four fifths of the left ureter was not visualized. There were no visible urinary calculi (Fig. 1). On July 17, the left

ureter was catheterized and 10 cc. of foul-smelling, turbid urine was recovered. Microscopic examination revealed many red cells but no organisms. Guinea-pig inoculation was negative for tuberculosis. On July 25, examination of a centrifuged specimen of urine revealed numerous white cells, many sulfadiazine crystals and a chemical determination of 218 mg. of sulfadiazine per 100 cc. The patient became afebrile soon after admission. On August 18, the ureters were again catheterized. The left kidney pelvis was irrigated with diluted acetic acid and a dark, grumous urine with heavy sediment was recovered. Following this a steady drip of clear urine was observed coming from the left ureter. Urograms revealed complete disappearance of the previously described dilatation of the left upper urinary tract, with normally appearing kidneys and ureters (Fig. 2). Following this the patient had an uneventful recovery, the urine cleared, the sedimentation rate fell, and blood urea nitrogen and renal-function tests returned to normal. The patient was returned to full duty on October 29.

SUMMARY

A case of hydronephrosis and hydroureter with recovery that occurred after prolonged obstruction by sulfonamide crystals is reported.

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MEDICAL PROGRESS

PANCREATIC INSUFFICIENCY AND THE CELIAC SYNDROME

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THE chronic failure of nutrition in infants and children described by Gee¹ in 1888 under the term "the coeliac affection" is recognized today as a syndrome rather than a disease entity always caused by the same etiologic factor. Only in recent years has an approach been made to an understanding of some of the conditions that produce the celiac picture. Gee himself remarked that "naked-eye examination of dead bodies throws no light upon the nature of the coeliac affection," and Parsons² in the Rachford Lectures described the results of pathological studies in true celiac disease as follows: "The finding, after much scratching about, of some small grains of reward in the shape of an alteration in a few cells does not seem sufficient to justify an exulting cackle, but rather should stimulate research in other directions."

Morbid anatomy has indeed thrown no light on the nature of the usually benign idiopathic celiac disease, but pathological studies have been responsible for a revival of intense clinical interest in the entire group of disorders bearing the celiac imprint. They have resulted, furthermore, in the discovery and characterization of clinical entities associated with pancreatic insufficiency in early life, including a condition until recently confused with idiopathic celiac disease. This condition, in contrast to what Parsons found in celiac disease, is characterized by important and easily demonstrable pathologic changes and is associated with pancreatic achylia produced by obstruction to the outflow of pancreatic juice. The present review will be limited to a consideration of this disorder, which has been variously termed "pancreatic insufficiency," "pancreatic steatorrhea," "pancreatic fibrosis," and "cystic fibrosis of the pancreas." The term "pancreatic achylia" will be used to describe the physiologic consequences of this obstructive lesion in the pancreas. Reference to true or idiopathic celiac disease will be made only when necessary for clarification of the subject matter. Results of studies at the Children's and Infants' hospitals, including unpublished data, will be drawn

on throughout this account. The contributions of Parsons² and of Neale,³ the monographs of Lehn-dorff and Mautner⁴ and of Fanconi⁵ and the recent summary of therapeutic and physiologic studies by May, McCreary and Blackfan⁶ should be consulted by the reader interested in idiopathic celiac disease and the celiac syndrome.

The features that characterize the celiac syndrome include the typical wasting, more in the limbs than in the face; distention of the abdomen, which may be soft, doughy and inelastic or markedly distended and tight; bulky, foul-smelling, frothy stools that contain excess fat; and often retardation of growth. To these may be added clumping of barium in the small intestine, a flat glucose-tolerance curve and a low rise in the level of vitamin A in the blood during the vitamin A-absorption test.⁶ These symptoms may appear as a result of congenital malformations of the small intestine or its attachment, chronic infections, dysentery, megacolon or pancreatic insufficiency. True or idiopathic celiac disease is used to describe this group of symptoms and laboratory findings in patients in whom no underlying disease can be found and who are improved and usually cured by treatment consisting of good general care and any one of the well-established celiac diets. Some idea of the difficulty of understanding the celiac syndrome may be obtained by reference to the large number of names applied to members of this group of diseases. These include acholia, intestinal infantilism, chronic intestinal indigestion, Heubner-Herter disease, Gee-Herter disease, pancreatic infantilism, chronic idiopathic steatorrhea, familial pancreatic insufficiency, indigenous sprue and pancreatic steatorrhea.

Since the time of Gee, true celiac disease has been differentiated with difficulty from a chronic failure of nutrition caused by pancreatic disease, with symptoms resembling those in true celiac disease so closely that the two conditions were considered by most observers to be identical. The striking nature of the clinical features of the celiac syndrome explains the neglect of the respiratory and other non-nutritional aspects of the disease associated with pancreatic insufficiency. The paucity of complete post-mortem studies and competent

The articles in the medical progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp., Spring 1941, Illinois: Charles C. Thomas, 1942, \$5.00).

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clinicopathological correlations is responsible for the late recognition of the fact that the celiac picture is only one of a group of what had been thought to be several unrelated diseases caused by or associated with an obstructive lesion in the pancreas that produces pancreatic achylia.

Beginning about thirty years ago, scattered post-mortem observations concerning the pancreas appeared in the literature on celiac disease. A marked increase in interlobular fibrous tissue of the pancreas, for example, was observed in 1914 by Poynton, Armstrong and Nabarro.⁷ Passini⁸ described actual pancreatic disease in an infant with nutritional failure. Some writers who found pancreatic lesions in patients with the celiac syndrome explained them as secondary to the failure of digestive secretion and function.⁹ The relation of pancreatic insufficiency to the celiac syndrome was brought into clear perspective in 1935 by a short clinicopathological communication by Parmelee,¹⁰ who referred to evidence gathered from the literature and reported 2 new cases of pancreatic disease. He suggested that what he called "congenital steatorrhea" differed from the usual picture of celiac disease in the early onset, the excessive amount of neutral fat in the stools and the uniformly fatal outcome. In these patients, at post-mortem examination there were found constant changes, including marked fibrosis and great diminution of secretory gland tissue in the pancreas, and bronchopneumonia, usually of a subacute type with purulent bronchitis and bronchiectasis. In 1935, Thaysen¹¹ grouped celiac disease, nontropical sprue and tropical sprue under the general heading of idiopathic steatorrhea. In the following year, Hanes and McBryde¹² stressed the identity of sprue and true celiac disease, and listed an impressive series of observations in favor of this conclusion. The logical analysis of Rauch, Litvak and Steiner¹³ paid particular attention to steatorrhea, which was classified as the idiopathic variety, which includes true celiac disease, and the pancreatogenous variety.

Several independent investigations published in 1938 and 1939 crystallized the problem and marked the beginning of the recent series of contributions to the present knowledge of the clinical characteristics of this pancreatic disease, the methods of diagnosis and treatment and the nature of the underlying disorder. Comprehensive reviews of the literature may be found in the papers of Andersen¹⁴ and of Rauch, Litvak and Steiner.¹³ In 1938, Andersen gave a detailed analysis of the clinical and pathological findings in 49 cases of pancreatic fibrosis, which included 20 from the post-mortem files of the Babies' Hospital, New York City. Her stud-

ies gave strong support to the validity of the separation of pancreatic fibrosis from true celiac disease and emphasized the logical use of pancreatic-enzyme analysis as a valuable diagnostic measure and of pancreatic substitution therapy. In the same year, Blackfan and May¹⁵ analyzed the clinical records of 35 cases selected from 2800 autopsies in the Department of Pathology of the Children's Hospital. These cases had been set apart as a pathologic entity because of the constant occurrence of an obstructive lesion of the pancreas, which was associated, however, with several different clinical pictures.

From the clinical analyses of Andersen and of Blackfan and May from a subsequent experience at the Children's Hospital,¹⁶ it appears that the infants in whom obstructive lesions of the pancreas are found at autopsy may be divided into three clinical groups: those who died either in the first week or first few weeks of life, usually from meconium ileus; those who died, usually in the first year of life, with a clinical history of nutritional disturbance often obscured by respiratory disease, usually called chronic pneumonia or bronchitis, or bronchiectasis; and those with symptoms recognizable as preceliac and celiac who died of respiratory disease.

Group 1. The term "meconium ileus" is used to describe intestinal obstruction in the newborn caused by the inability of the intestine to propel through its lumen a thick, mucilaginous meconium, the altered physical state of which is explained by the failure of pancreatic enzymes, particularly trypsin, to act on it during intra-uterine life.¹⁷ Death has occurred almost invariably in infants with this severe type of intestinal obstruction. Lesser degrees of obstruction may be produced by inspissated meconium unassociated with pancreatic achylia, as in stenosis of the ileocecal valve. Post-mortem examination of patients with true meconium ileus reveals pancreatic fibrosis with obstruction to the outflow of secretions proved in some cases to be caused by congenital atresia or stenosis of the main pancreatic ducts. Absence of tryptic activity in the pancreatic juice has been demonstrated in one patient with meconium ileus, and in the duodenal content obtained at autopsy shortly after death in another. Dilute solutions of pancreatin added to the grossly altered mucilaginous meconium bring this material to a watery consistence. Successful attempts have been made to relieve the intestinal obstruction in meconium ileus by introducing a 1 per cent solution of pancreatin directly into the duodenum so that it may act on the altered meconium.¹⁷ Recent reports of meconium ileus have been made by Hurwitt

and Arnheim¹⁸ and by Kaufmann and Chamberlin,¹⁹ who review the literature

Group 2. Andersen¹⁴ found that patients in this group usually died before six months of age, and that many of them presented feeding problems characterized by hunger, failure to gain weight and foul, bulky stools. A somewhat different summary was given by Blackfan and May,¹⁶ who recognized that the clinical manifestations in this group were limited in variety but were common to so many disorders in infancy that a sharply defined clinical picture could not be drawn. Usually, these infants developed symptoms referable either to the gastrointestinal tract or to the respiratory system. Vomiting and diarrhea with failure to gain weight or loss of weight preceded the onset of signs of infection of the respiratory system in some cases, but in others a severe and nonproductive cough was an early complaint, followed later by a productive cough and physical signs of partial or complete obstruction of different parts of the bronchial tree. Vomiting was usually not present. Diarrhea was occasionally severe and often lasted for prolonged periods. The stools contained no pus or blood and were definitely not fatty. The average duration of the illness of the patients who lived beyond the neonatal period was six months. The average age at death in this group was eight months. The pertussis-like cough impressed Rauch and his co-workers¹³ as a characteristic feature of this disease.

Group 3. About half the patients in Andersen's¹⁴ series fell into this group, and ranged in age from six months to fourteen and a half years. They all died of pulmonary infection. Only one fifth of the patients described by Blackfan and May¹⁵ were included with these cases, which possessed clinical features similar to those of true celiac disease, such as emaciation, distention of the abdomen and large, pale, putrefactive, fatty stools. All these patients died of pulmonary disease.

In our experience,¹⁰ Group 2 is by far the largest and the cases in it are the most difficult to recognize, and Group 3 in which the condition closely resembles that of true celiac disease, is the smallest. It appears that the patients in all groups are apt to die before there is developed a clinical picture that can be confused with true celiac disease. It is probable that, as further experience with the disease is gathered, the cases in Group 2, in which the respiratory symptoms dominate the picture, will be divided into more distinctive clinical branches.

The familial aspect of this disease has been recognized. A number of cases have been re-

corded of two or three siblings with the same disease, as proved either by post-mortem examination or by pancreatic-enzyme analysis. The early onset of symptoms has caused the disease to be regarded as congenital.

It is probable that this pancreatic disease is much commoner than may be concluded from the number of cases reported in the literature. Andersen¹⁴ found an incidence of 3 per cent in her post-mortem records. Blackfan and May¹⁶ reported an incidence of 13 per cent among infants and children examined at autopsy up to 1937 at the Children's Hospital. In the same laboratory during the following six years ending with 1942, 52 cases of marked pancreatic fibrosis (48 per cent) were found among 1089 autopsies on infants and children, with meconium ileus in 13; in 1942, autopsies were performed on 198 cases, of which 16 (12 per cent) showed pancreatic fibrosis.²⁰ Early cases of the lesion consisting in inspissation of secretions only in the acini are now being frequently found in routine post-mortem studies on infants and children.¹⁰

PATHOLOGICAL FINDINGS

The lesion in the pancreas seen most frequently in these patients is characterized by dilatation of ducts, inspissation of secretion, atrophy of acinar structures and replacement of connective tissue, leading to marked fibrosis of the organ.^{14, 16} Congenital stenosis or atresia of the pancreatic ducts may be found. In most cases, obstruction appears to begin in the acini. The islets of Langerhans are not involved. The lesion may be recognizable grossly or may be complete histologically and functionally without visible gross change. No matter what the cause of the lesion, the effect of obstruction within the acini themselves is equivalent to that produced by ligation of the main pancreatic ducts. From this histologic picture, interference with the production, liberation or passage of pancreatic enzymes leading to pancreatic achylia may be expected.

Hyperexpansion and atelectasis, usually in combination, are the commonest early findings in the lungs, and these are explained by obstruction caused by the tenacious mucopurulent material usually found in the upper respiratory tract. In the more advanced cases of the disease, widespread bronchiectatic and bronchiolectatic abscesses are found. *Staphylococcus aureus* is usually the offending organism. Thickening of the bronchiolar walls, replacement fibrosis in those areas of the lungs repaired after staphylococcal destruction and diffuse bilateral acute and chronic bronchopneumonia characterize the later stages of the disease. Fundamentally the process in the lung is one of upper respiratory obstruction caused by thickened,

tenacious mucus, with secondary infection by *Staph. aureus*.¹⁶

Three explanations for the pulmonary lesions have been offered. Decreased resistance in a chronically ill patient with nutritional failure is an obvious conclusion. Secondly, metaplasia of bronchial epithelium caused by vitamin A deficiency has been held responsible for the secondary infection that follows mechanical obstruction and loss of ciliated epithelium.¹⁴ This plays a role, but only in patients with evidence of vitamin A deficiency of important degree. The third explanation depends on the thick mucus produced in the tracheal and bronchial glands, which fails to lubricate properly the ciliated epithelium of the upper respiratory tract and so permits infection by a staphylococcus of low virulence.¹⁶ More important than the infection is the obstruction caused by the tenacious mucus, comparable in consistence to the viscid pancreatic juice found in the duodenal content. This obstruction is the cause of most of the early signs of respiratory disease and is responsible for the bronchiectasis and later the bronchiectatic abscesses.

The liver is usually increased in size and shows fat metamorphosis. In rare cases there is an unusual form of biliary cirrhosis characterized by a lesion resembling closely that in the pancreas.²⁰ Inspissation of secretions in the ducts and acini of the salivary glands and in the mucous glands of the trachea, bronchi, esophagus and gall bladder occurs with such frequency that it must be regarded as a characteristic feature of the disease.¹⁶ Other evidences of general, severe disturbances in nutrition and vitamin deficiency may be recognized elsewhere in the body—for example, in the skeleton, in the wasting, hypertrophy of muscles, in the disappearance of fat from the fat depots and in the general retardation of growth. Keratinizing metaplasia in the upper respiratory tract, pancreas, salivary glands or renal pelvis, characteristic of vitamin A deficiency, is occasionally but not regularly found.^{14, 16}

ETIOLOGY

Pancreatic achylia may be caused by congenital atresia or stenosis of the pancreatic ducts, or congenital malformation of the duodenum and head of the pancreas.^{14, 16} Congenital syphilis causing widespread fibrosis of the pancreas or intrauterine infection of unknown etiology producing obliteration to the duct system may well be responsible in some cases. In the majority of cases, however, the pancreatic achylia is unassociated with any such gross congenital anomalies or inflammatory lesions obstructing the outflow of pancreatic juice.¹⁶ To clarify the pathogenesis of the lesion producing pancreatic achylia in this large group of infants

and children, three causes have been suggested; namely, vitamin A deficiency, a filterable-virus infection and a fundamental alteration in the physical character of the acinar secretion.

A deficiency of vitamin A may be responsible for gross obstruction of the pancreatic ducts,¹⁴ but this is a rare event.¹⁶ Following metaplasia of the epithelium of the duct lining to a stratified squamous type, there may be complete filling of the ducts by masses of desquamated, keratinized epithelial cells. Some evidence of vitamin A deficiency on histologic examination of certain organs, not necessarily including the pancreas, was found by Andersen¹⁴ in 23 per cent of the cases studied or collected. In our own experience,¹⁶ evidences of vitamin A deficiency were less frequent than this. Although there is a defect in the absorption of vitamin A associated with this pancreatic disease, it must now be regarded as merely one of the complications of the disease process, not of primary importance in the pathogenesis of the pancreatic lesion but responsible for some of the symptoms and laboratory findings.¹⁶

The frequent occurrence of chronic bronchopneumonia in infants with pancreatic disease of this type and the finding of inclusion bodies in certain cases have justified further investigation of the possible role of a filterable virus in the etiology of this condition. Brody²¹ has recently reported the finding of inclusion bodies in 2 of 3 patients with pancreatic fibrosis. Experimental support for this suggestion is still lacking. A review carried out with the assistance of Dr. Edward Pratt²² of 50 post-mortem examinations of infants who suffered from a severe degree of this pancreatic disease disclosed intranuclear and cytoplasmic inclusions in the salivary glands, lungs, trachea or pancreas in 6 (12 per cent) of the series. This is no greater than the incidence of cytoplasmic and intranuclear inclusion bodies in the total number of autopsies in the same laboratory.²³ These studies, therefore, provide no support for the suggestion that a virus disease is of primary importance in the causation of this pancreatic lesion, although secondary effects from a possible superimposed virus infection cannot be excluded.

The prominence of the inspissated secretions in the pancreas in this disease suggested to Blackfan and Wolbach²⁴ in 1933 that this striking lesion could be attributed to the production of an abnormal pancreatic secretion. Study of 87 cases of the advanced lesion and about 350 cases of early stages of the process support the hypothesis that the basic lesion consists in a physically altered pancreatic secretion, which causes intrinsic obstruction in the acini and small ducts, finally leading to dilatation and obstruction in the larger ducts.^{16, 20} Atrophy

of the acinar structures follows, and condensation of the connective-tissue framework of the pancreas secondary to loss of parenchyma, combined with an ingrowth of new fibrous tissue, gives the picture of diffuse fibrosis. Support for this theory comes from the observation that the fully developed clinical picture of the celiac syndrome may exist and the pancreatic enzymes in the duodenal contents may be markedly reduced at a time when the sole lesion in the pancreas consists of inspissation of secretion in the acini and small ducts, with no evidence of atrophy of the parenchyma, fibrosis or dilatation of the large ducts.²⁵ Further evidence of the abnormality of the pancreatic secretion is given by the gross appearance of the scanty, extremely thick and viscid pancreatic juice obtained when the duodenal contents are collected for enzyme analysis, as contrasted with the thin, watery pancreatic juice obtained from normal infants or from those suffering from true idiopathic celiac disease.²⁵

Inspissation of secretions and dilatation of glandular structures of the same general character as these alterations in the acini and small ducts of the pancreas are found at autopsy on these patients in the glands of the trachea, bronchi, esophagus, duodenum, gall bladder and intestinal tract. Inspissation of bile to a degree sufficient at times to cause intrahepatic biliary obstruction may also occur. These findings suggest that the inspissation of altered secretions in the pancreatic acini is only a part of a generalized disorder of secretory mechanisms involving many glandular structures but exerting its greatest effect on the pancreas.¹⁶ In experiments on kittens, suggested by this conception of the pathogenesis of the pancreatic lesion, it has been possible to produce, by the administration of parasympatheticomimetic drugs (pilocarpine and Mecholyl), the histologic picture of inspissation of secretions in the acini and small

ducts in the pancreas and the clinical picture of a severe chronic nutritional disturbance.¹⁶ The cause for this suggested disturbance of the secretory mechanism in the pancreatic acini of infants remains to be demonstrated.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

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CASE 29421

PRESENTATION OF CASE

A forty-one-year-old night watchman was admitted to the hospital because of intermittent gas pains of ten years' duration.

The patient was apparently well until about ten years prior to entry, when he developed intermittent attacks of indigestion in which he suffered from epigastric gas pains and the sensation that his stomach was "tied up in knots." The pain occurred approximately half an hour after eating, or when he had gone three or more hours without eating, and lasted for about an hour. It was relieved by anything that would "break the gas" and produce gaseous eructations, such as soda, milk or food. The attacks were sometimes precipitated by cabbage, pork and fried foods. Vomiting of undigested food, especially fried food, sometimes gave relief. The vomitus was never bloody, nor did it contain coffee-grounds material. The last attack of vomiting occurred six weeks before admission. Three years before admission, following x-ray examination at a community hospital, he was placed on a strict ulcer regime, with prompt symptomatic relief as well as gain in weight. The diet, however, was discontinued six months later and the symptoms recurred. Nine months prior to entry, while working in a dusty atmosphere, he had two or three attacks of vomiting and his symptoms increased in severity for two months, at which time he obtained another job, with some relief in his condition. In the three or four months before entry he experienced daily distress after almost every meal. There was anorexia and a weight loss of 15 pounds. He subsisted mainly on soups, milk and cream, crackers, tea and so forth. He became progressively weaker.

He had been constipated most of his life and had habitually taken various laxatives. There had been no back pain, heartburn, dizziness or fainting. He smoked one package of cigarettes daily and drank some beer and a little whisky. He had experienced considerable financial difficulties.

Physical examination showed a well-developed,

small, wiry, tense man, with evidence of recent weight loss. There was no pallor. He was edentulous. The tongue was reddened and coated with coarse papillae. The heart and lungs were normal. The abdomen was scaphoid and soft. There was no tenderness, spasm or palpable masses. Peristalsis was active. Rectal examination revealed a small, firm, nontender prostate. Considerable tenderness was elicited superiorly and on the left, where a questionable soft mass was palpated.

The blood pressure was 125 systolic, 80 diastolic. The temperature was 98.6°F., the pulse 76, and the respirations 20.

The blood showed a red-cell count of 4,300,000, with a hemoglobin of 14 gm. The white-cell count was 6800, with 63 per cent neutrophils. The urine was normal. The stools were guaiac negative on eight occasions but gave a +++ test on one occasion. The blood Hinton test was negative. The nonprotein nitrogen was 20 mg. per 100 cc. The blood protein was 5.6 gm. per 100 cc., the carbon dioxide combining power 21 millimols per liter, the chloride 95.9 milliequiv. per liter and the blood sugar 74 mg. per 100 cc. Gastric analysis showed no free acid before and half an hour after histamine injection; the values for total acidity were 5 and 18 units respectively. Both aspirations gave a ++ guaiac test.

X-ray examination showed a normal esophagus. Just below the cardia there was an ulcer crater measuring 1 by 1 cm., with a rigid, soft-tissue mass surrounding it. This filling defect measured 4 cm. in length. The remainder of the stomach and duodenum was normal.

The patient was placed on a gastric diet with tincture of belladonna, 15 drops, and phenobarbital, 2 gr., three times a day. His condition improved. Gastroscopic examination eight days after entry showed a normal antrum and pylorus and an increased reddening of the body of the stomach in the upper part, with a few streaks of bright-red blood. There was a marked verrucous, cobblestone appearance in the upper 4 or 5 cm. near the cardia; no ulcer crater could be demonstrated. Following gastroscopy, the epigastric symptoms recurred but were relieved by Creamalin, 45 cc. every two hours. A gastric analysis on the fifteenth day showed 25 units of free acid and a total acid of 35 units half an hour after histamine injection. X-ray examination after one month on the medical regime showed the ulcer crater to be smaller than it was formerly, but the crater was surrounded by what appeared to be a polypoid mass extending along the lesser curvature for about 8 cm. The lesser curvature was rigid in this area.

An abdominal exploration was performed six days later.

*On leave of absence.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM B. BREED: It seems to me that there are two possibilities to be considered. Either this lesion was a benign one throughout its course or it started as a peptic ulcer, then degenerated and became malignant. The history certainly is suggestive of the latter supposition. You will note that the early story is indicative of peptic ulcer with periodic pyloric obstruction and relief of symptoms on an ulcer regime, as well as recurrence of symptoms when the regime was discontinued.

The dusty atmosphere of his new job can be disregarded. I have no thoughts about that.

Two or three months prior to entry he began to have continual discomfort directly after eating, with anorexia and loss of weight but no typical symptoms of ulcer. Up to that point this could well have been a benign ulcer near the cardia that had degenerated and had become malignant. Gastroscopy possibly confirmed the nature of the process: the upper part of the stomach wall was verrucous and cobblestone in appearance.

DR. EDWARD B. BENEDICT: That does not mean malignant disease. That means gastritis.

DR. BREED: I am glad you are here, Dr. Benedict. The record states, "a marked verrucous, cobblestone appearance." There was no mass? Will you describe it as you remember it?

DR. BENEDICT: A verrucous and cobblestone appearance may mean chronic hypertrophic gastritis.

DR. BREED: In a localized area?

DR. BENEDICT: Sometimes localized, sometimes generalized. This was fairly well localized.

DR. BREED: You introduce the idea here at once that this lesion was benign. Let us go ahead and see whether we can put that together with the second examination by x-ray, which described a polypoid mass extending along the lesser curvature, with a rigid mucosa.

In passing, I should say that one has to consider lymphoma of the stomach in any condition like this. However, I am willing to conclude that if this was a polypoid mass it probably was not due to lymphoma. Do you ever see polyps in lymphoma, Dr. Benedict?

DR. BENEDICT: Not discrete polyps.

DR. BREED: You saw no polypoid mass?

DR. BENEDICT: No, but I could not see the ulcer. It was in a part of the stomach that is difficult to visualize.

DR. BREED: No polyp was seen on the first x-ray examination. We might see both sets of film.

DR. MILFORD SCHULZ: Here are the films made at the time of admission, and there is no gain saying the fact that there is an ulcer with what appears to be a mass of soft tissue about it. In

addition you can see an irregular soft-tissue mass extending into the cardia.

DR. BREED: What does that mean to you? Is this soft-tissue infiltration?

DR. SCHULZ: By all the rules it should be a carcinoma.

Here are the films made after a month of treatment. The ulcer is somewhat smaller. You still see all this thickened verrucous soft tissue extending into the air-filled and barium-filled portion of the stomach. It is true that there are quite prominent mucosal folds throughout the stomach; in a recent similar case, however, in which a diagnosis of cancer was made, the condition at operation proved to be gastritis and not carcinoma.

DR. BREED: This is not that case by any chance?

DR. SCHULZ: No.

DR. BREED: Kindly show me the polyp.

DR. SCHULZ: There is no true polyp, but there are numerous soft-tissue masses extending into the gas bubble of the stomach and displacing the barium. Here is the defect in the stomach in which the ulcer lay. By all the rules that should be a neoplasm.

DR. BREED: I am going to stick to the rules, because it is a fairly straightforward history and I see no reason for trying to be too smart. The patient had an ulcer for ten years and then developed a cancer at the site of the ulcer.

DR. BENJAMIN CASTLEMAN: Is there any other comment?

DR. J. H. MEANS: I think it could be a leiomyoma. I am not offering that as one of the possibilities, but it seems to me that I recall that they are apt to run a more or less benign course for some years and then become increasingly malignant.

DR. CASTLEMAN: They usually give a long history of bleeding and become larger extremely slowly. A few of them do become malignant, however.

DR. MEANS: What about other tumors of the stomach, such as fibroma?

DR. CASTLEMAN: I do not believe that an accurate differential diagnosis of the various intramural tumors—fibroma, neurofibroma and leiomyoma—can be made clinically or by x-ray, or even microscopically in some cases.

DR. MEANS: I discussed that point with Dr. George W. Holmes some years ago. He claimed that when they were smooth and round it was one thing, and when lobulated it was another. How about the significance of these differences? Does the lobulation mean anything?

DR. CASTLEMAN: A definite lobulation is perhaps more in favor of a neurofibroma, but all these

tumors tend to be well circumscribed and round. They often have a central ulceration.

DR. SCHULZ: An intramural tumor is usually quite characteristic in appearance roentgenologically. It displaces or smooths out the mucosa rather than showing soft-tissue masses extending into the lumen of the stomach.

DR. BREED: I shall have to add that he had gastritis as well as cancer.

DR. BENEDICT: I think the ten-year history is in favor of a benign lesion.

DR. BREED: Such as?

DR. BENEDICT: Benign ulcer. Of course that brings up the question, Do benign ulcers ever become malignant? A lot of people think that they never do.

DR. CASTLEMAN: I was about to take issue with Dr. Breed's statement.

DR. BREED: I have two against me.

DR. CASTLEMAN: We are certain that an ulcer remains an ulcer and does not degenerate into a carcinoma. I believe that there are a few cases with definite ulceration in the stomach, proved roentgenologically, that ten years later develop carcinoma in the same location—that is, in the ulcer. If one checks some of these histories of long-standing ulcer with carcinomatous degeneration one often discovers that the ulcer was in the duodenum and not in the stomach, and things of that sort. It is true that carcinoma can remain in the precancerous state,—carcinoma in situ,—limited to the mucosa, without invasion over a long period of time. We have seen several examples of this condition.* Furthermore, precancerous lesions have been known to exist for six or seven years in the cervix. These carcinomas in situ may ulcerate; they are, however, ulcerating carcinomas, rather than carcinomas developing in benign ulcers.

DR. BREED: Along that line, it did occur to me when I was studying this case that the patient might have had a duodenal ulcer and that this was a new malignant lesion. I am willing to go back to that idea. Since the pathologist insists that ulcers do not degenerate, I shall probably have to agree; but I still think that the lesion was malignant.

DR. MEANS: The picture could fit with carcinoma in situ, could it not?

DR. CASTLEMAN: It could, although ten years is a long time for carcinoma in situ; most of them are under five years in duration.

DR. RONALD C. SNIFFEN: This area of the stomach is rather unusual for carcinoma in situ, is it not?

*Mallory, T. B. Carcinoma in situ of stomach and its bearing on histogenesis of malignant ulcers. *Arch. Path.* 30:348-362, 1940.

DR. CASTLEMAN: Yes; most of the lesions have been in the prepyloric region.

DR. BREED: The patient may have had a duodenal ulcer for ten years and then developed cancer of the stomach in the cardia. I am willing to accept that.

CLINICAL DIAGNOSIS

Carcinoma of stomach.

DR. BREED'S DIAGNOSES

Carcinoma of stomach.

Duodenal ulcer?

Chronic gastritis.

ANATOMICAL DIAGNOSIS

Acute and chronic phlegmonous gastritis, with gastric erosions and ulcerations.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The surgeon's operative notes state that he was able to feel two ulcers, one close to the cardia and one 5 or 6 cm. below that. He thought that the lesion was probably benign, but since he was not absolutely sure, and since the ulcers were high in the cardia, he believed that the patient would do better by having a resection.

When the stomach was opened, we found innumerable ulcers. Some were old, measuring 2 or 3 mm. in diameter, with a greenish-fibrinoid base, the result of necrosis. Between the ulcers the mucosa was markedly edematous and red and the rugae were prominent. This appearance reminded me of that of ulcerative colitis, with bridges between the ulcers. It might be called a phlegmonous gastritis.

Microscopic sections showed an acute and chronic inflammatory reaction throughout the whole wall, with necrosis of the mucosa and the formation of erosions and deep ulcers. We were unable to find a chronic ulcer that the patient might have had for ten years. It may have been in the duodenum, or the more recent disease may have covered it.

DR. BENEDICT: Were they true peptic ulcers, or erosions?

DR. CASTLEMAN: Both were present.

DR. BENEDICT: How do you distinguish between them?

DR. CASTLEMAN: One speaks of an erosion if the destruction extends to the muscularis mucosa; if it goes beyond that, it is an ulcer. The etiology is the same.

There was no evidence of malignant disease.

CASE 29422

PRESENTATION OF CASE

A fifty-four-year-old press operator entered the hospital because of uterine prolapse.

The patient had been in good health all her life. She had had four pregnancies, only two of which terminated successfully. About eight years before admission she was told by her physician that she had prolapse. About the same time she developed increased frequency and occasional slight incontinence. There was no nocturia. About one year before entry she noted protrusion of a mass between her legs. At first the mass appeared after prolonged standing and on coughing or exertion. The prolapse increased in amount and she developed low abdominal pain, slightly increased urinary frequency and occasional slight incontinence. There was nocturia (one to three times). She had lost 30 pounds during the year before entry.

Physical examination showed an obese woman in no distress. The fundic vessels were tortuous, and there was moderate arteriovenous nicking. The lungs were clear. The heart was normal. The sounds were regular and of good quality. The liver edge was palpated two fingerbreadths below the costal margin. There was an "enormous" rectocele, with an ulcer on the posterior vaginal wall near the cervix and another on the cervix. A large cystocele was also present. The fundus of the uterus was not particularly enlarged; it was palpated almost at the level of the introitus.

The blood pressure was 184 systolic, 110 diastolic. The temperature was 99.2°F, the pulse 88 and the respirations 20.

Examination of the blood showed a hemoglobin of 90 per cent and a white-cell count of 12,250. Urinalysis revealed a ++ test for albumin; the sediment contained 3 white cells per high-power field. The blood Hinton test was negative. A urine culture was negative. A vaginal culture showed colon bacilli, *Staphylococcus aureus* and beta-hemolytic streptococci.

On the third hospital day a vaginal hysterectomy and perineorrhaphy were performed under ether and nitrous oxide anesthesia. During the course of the operation, which lasted three hours, the blood pressure fell to 80 systolic, 40 diastolic, with a rise of pulse to 100. With intravenous fluids, however, the pressure gradually rose to 100 systolic, 70 diastolic, at which level it remained the last hour of the operation. At the end of the operation she was given 500 cc. each of plasma and blood, with a subsequent rise of systolic blood pressure to 220.

Following operation, the patient failed to regain consciousness or even respond to painful stimuli.

Examination revealed absence of motion in any part of the body. The neck was not stiff. The abdomen and heart were not "too remarkable." There was no upward motion of the eyes, which remained fixed, looking straight ahead. The pupils were dilated, measuring 4 mm. in diameter. They were round and regular but failed to react to light. The face was flat, flabby, symmetrical and motionless. The tongue moved when stimulated. The muscles of the extremities were symmetrical. A slight increased resistance to passive stretch was noted in the right leg. There were no adventitious movements. No reaction to pinpricks could be elicited. The biceps, triceps, radial, knee and ankle reflexes were "very lively," with increased knee jerks on the right. Bilateral ankle clonus and Babinski reflexes were present, and there was an increased Hoffmann sign on the right. The non-protein nitrogen was 18 mg. per cent, and the chloride 100.3 milliequiv. per liter.

The patient remained unconscious, and died twenty hours after operation.

DIFFERENTIAL DIAGNOSIS

DR. JULIA G. ARROWOOD: This discussion should answer two questions: By what accident or mechanism did this catastrophe occur? Was it possible to foresee and prevent it? Since at these meetings we desire to arrive at the final diagnosis as a sort of climax, let us first examine the somewhat meager information we have in search of an answer to the second question.

The patient was obese, arteriosclerotic and hypertensive. The cardiac examination is disposed of in two sentences. "The heart was normal. The sounds were regular and of good quality." With a diastolic pressure of 110, I should be inclined to expect some cardiac enlargement and hypertrophy. It is stated that she had nocturia. How did the quantity of day and night urine compare?

DR. BENJAMIN CASTLEMAN: There is no further statement in the record.

DR. ARROWOOD: Was there a cardiac consultation or an electrocardiogram?

DR. CASTLEMAN: No.

DR. ARROWOOD: The temperature of 99.2°F. and the white-cell count of 12,250 can be explained by the ulcerated condition of the large cystocele and rectocele. It would be interesting, however, to know if she had a daily elevation of temperature during the preoperative hospital stay.

DR. CASTLEMAN: The temperature on admission was 99.2°F. It fell to normal the following day and remained so during the entire preoperative period.

DR. ARROWOOD: Whether or not this death could have been foreseen and prevented, one can

only say that patients of this type are notoriously poor risks, and that their cardiac status should be carefully investigated before surgery is undertaken.

It is obvious that during the operative period this woman must have had an episode of cerebral anoxia, which resulted in complete functional decerebration. The persistent coma, with absent superficial reflexes, hyperactive deep reflexes and the presence of bilateral ankle clonus and Babinski reflexes, indicates widespread cerebral damage. It seems likely that this may have occurred in one of three ways: from asphyxia following overdosage of the anesthetic agent, from respiratory obstruction or from a cerebrovascular accident during the operation.

There is no mention of any untoward happening, but I would like some additional information about the course of anesthesia. Was the induction satisfactory? Was there cyanosis, obstruction or respiratory difficulty at any time? What was the anesthetist's estimate of the anesthesia and of the patient's condition at its close? I assume, however, that there was no period of acute respiratory failure to account for the patient's condition.

The second possibility is that the cerebral damage was produced by hypoxia lasting over a considerable period of time. The lithotomy position in an obese patient causes considerable embarrassment to respiration by pressure of the abdominal contents against the diaphragm. The operation lasted three hours, and the blood pressure fell to 80 systolic, 40 diastolic. In this connection, I should like to know what the initial blood-pressure reading on the anesthesia sheet is, and when the fall occurred. It is stated, "The pressure gradually rose to 100 systolic, 70 diastolic, at which level it remained the last hour of the operation." What was the blood pressure on the patient's return to the ward, and how long was it before it reached a more nearly normal level—say 130 systolic, 80 diastolic? My point is that hypoxia from respiratory embarrassment due to position, combined with a blood pressure that was very low for this patient, whose blood-pressure reading on the ward was 184 systolic, 110 diastolic, might have been sufficient to produce the fatal brain damage.

The third possibility is that the patient had a cerebrovascular accident during the time of anesthesia and operation. This could have been a massive hemorrhage with continued bleeding, reaching proportions sufficient to cause the extensive damage that occurred. It is quite conceivable that there had been previous coronary disease with cardiac infarction and mural thrombosis and such a cardiac thrombus could have been the origin of a cerebral embolus, which in turn formed the basis

for a growing thrombus. Finally it is possible that during the long period of hypotension in this arteriosclerotic patient, a thrombus could have originated in a cerebral vessel, the early signs being masked by the anesthesia.

To be specific concerning my diagnosis, I do not believe that the patient had any episode of acute anoxia to account for her death, but that she had a cerebrovascular accident, either thrombosis, hemorrhage or embolus. I do not believe it is possible to differentiate these with the evidence we have, but my guess is in the order named.

DR. CASTLEMAN: Dr. Brenizer, you saw this patient during operation. Will you tell us about the case?

DR. A. G. BRENIZER: The patient had good color throughout the operation. There was no cyanosis or anything like that, just a drop in blood pressure uncontrolled by intravenous fluids.

DR. RICHLARD H. SWEET: Was the intravenous solution running before or after the fall in blood pressure had occurred?

DR. BRENIZER: It was started as soon as we were notified that the blood pressure was falling. The 5 per cent dextrose and physiologic saline solution was changed over to plasma as soon as possible.

DR. SWEET: Was there much loss of blood?

DR. BRENIZER: I should say moderate.

DR. SWEET: There is apt to be with that type of operation.

DR. CHARLES S. KUBIK: Was there anything else to indicate that something had happened suddenly? Was the drop in blood pressure rapid?

DR. BRENIZER: The drop in blood pressure was rather sudden.

DR. FREDERIC B. MAYO: In answer to Dr. Arrowood's question concerning neurologic opinion, three diagnoses were considered: thrombosis at the time that the blood pressure dropped; hemorrhage when the blood pressure rose so high; and cerebral anoxia, which was subsequently ruled out by information that anesthesia was uneventful.

DR. SWEET: One of the conditions that I fear most in practicing surgery is the marked drop in pressure from ether or nitrous oxide anesthesia in a person who has or may have cardiovascular disease, especially those with hypertension. This patient probably had hypertension, and the fall to the level that she reached is, in itself, enough to explain the things that happened to her. The possibility that such an accident may occur is one reason why many of us do not use spinal anesthesia in patients of that sort.

DR. JACOB LERMAN: Sudden rise in systolic blood pressure from a low level to 220 suggests a rapid increase in intracranial pressure. That would per-

haps fit more with subarachnoid than with cerebral hemorrhage.

CLINICAL DIAGNOSIS

Cerebral anoxia.

DR. ARROWOOD'S DIAGNOSIS

Cerebrovascular accident (thrombosis, hemorrhage or embolus).

ANATOMICAL DIAGNOSES

Cerebral embolus, left middle cerebral artery.

Cerebral infarction with temporal pressure cone

Subacute bacterial endocarditis, mitral valve

Chronic rheumatic endocarditis, with stenosis of mitral valve.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy this patient showed a cerebral embolus, which Dr. Kubik will describe. The heart was moderately enlarged, weighing 370

gm. There was a marked degree of mitral stenosis, on which was superimposed a subacute bacterial endocarditis that must have been present long before operation. A thrombus had undoubtedly broken off and entered the brain.

DR. CHARLES S. KUBIK: The embolus was in the left middle cerebral artery, and infarction of a large portion of the left cerebral hemisphere corresponding to the distribution of the occluded artery had occurred. An unusual feature was marked swelling of the left hemisphere, with herniation of the hippocampal gyrus into the notch of the tentorium and resulting compression of the midbrain. The aqueduct was flattened, and there were small hemorrhages in the midbrain. The herniation, or temporal pressure cone, through its effect on the midbrain unquestionably accounted for the dilated fixed pupils and for the bilateral extensor plantar responses and was probably responsible to a large degree for the deep state of coma and eventual fatal outcome

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FOREIGN RELIEF AND REHABILITATION

WAR can leave little but disaster in its wake, and it is to offset its miseries so far as possible and as quickly as possible that the Office of Foreign Relief and Rehabilitation Operations was organized. This organization, under the directorship of former Governor Lehman, of New York, has recently reported on activities of the medical personnel attached to its North African mission, and described its preparations for medical and sanitary measures in future relief theaters.

In North Africa, public-health officers assigned

to OFRRO by the U. S. Public Health Service have been working with the North African relief and rehabilitation mission for the past six months, gaining valuable experience in medical relief. They have been attached by General Eisenhower to the military command, in charge of activities affecting civilian health, and they work through the French civil authorities, utilizing existing health and governmental services and professional personnel.

Acting in a military capacity, members of the OFRRO serve practically as public-health officers of the Army. Thus, medical personnel of the mission entered Tunis within twenty-four hours after the city's fall, establishing sanitary controls for the region, and the same was done in the Panteliera and Lampedusa campaigns.

Among the varied duties of the medical personnel of OFRRO have been assisting the French authorities in obtaining lend-lease medical supplies, helping to restore normal health service in cities and rural districts, advising in the creation of modern health departments, as was done at Oran, establishing de-lousing stations to check the spread of typhus, and disinsecticizing airplanes to prevent the spread of insect-borne disease.

Meanwhile, in order that future relief programs in distant theaters may be expeditiously carried out, different types of standard packaged units of medical supplies are being assembled in the United States for immediate shipment to any area. Thus, one basic unit containing the minimal medical supplies required for the control of the more frequent diseases of world-wide occurrence is designed to meet the needs of a group of 100,000 people for a one-month period, and includes some one hundred and fifty items. A larger unit, containing approximately fifteen hundred items, is planned to care for a group of 1,000,000 people for a three-month period. Supplemental packages are designed to combat epidemic disease, or conditions peculiar to certain regions.

In addition, standard hospital units have been prepared. One includes the essential equipment

for a 50-bed hospital, and another that for a 150-bed hospital. Laboratory units contain equipment for an epidemic-control laboratory, an emergency field laboratory, a laboratory for a 50-bed or a 150-bed hospital, a central pathological laboratory and a laboratory supply center. A few public-health teams are also being recruited, a typical team being made up of a health officer, a sanitary engineer, a pediatrician, a medical nutritionist, a medical supply officer, a nursing specialist, a malariologist, if necessary, and a hospital nutritionist.

Our nation, more power to it, has always been eager to spread its good works abroad. In the excitement of rebuilding the Eastern Hemisphere, however, we must not lose sight of our own problems that are just causes for anxiety and concern. In eventually putting our own house in order we must accept the challenge of a rising venereal-disease rate; we must cope with an influx of tropical diseases; we must face, far more intelligently and humanely than we have yet done, the problem of rehabilitation of many thousands of young men rejected by their draft boards or discharged from the army as unfit for further military service; and, last but not least, we must provide some means, other than that proposed by Senators Wagner and Murray, for improving the health of the people of the Nation.

SHOCK THERAPY

The brilliant results obtained by the use of plasma and plasma substitutes in shock are well known and occupy an important place in modern war surgery. But investigators have not limited their observations to this one therapeutic method.

The question whether to warm or cool the patient in shock has recently received considerable attention. First-aid courses continue to teach that the application of external heat is a cardinal principle in the treatment of shock—indeed it is practically the only method of therapy (except leaving the patient alone) that may be practiced by the first-aid worker; and it is often assumed that a patient cannot be overheated so long as his

skin is not burned by hot applications. Yet all current reports that bear on the subject clearly indicate that the overzealous application of heat is harmful in shock. This is equally true whether it is due to burns,¹ trauma or hemorrhage.² Indeed, a little thought along physiologic lines makes this obvious. Shock is a state in which the circulating blood volume is inadequate, with resulting anoxia. The local application of heat produces cutaneous vasodilatation, and this, in turn, causes the blood volume to become even more inadequate, owing to the greater vascular bed; furthermore, an increase in tissue metabolism resulting from warming the whole body increases the anoxia, and sweating augments dehydration. It therefore seems unwise to use hot-water bottles, heating pads and other sources of external heat to such an extent that the internal temperature of the body is raised above normal levels. As a matter of fact, induced hyperthermia may reproduce the shock syndrome.

As a corollary, it might be supposed that cooling of the body would be beneficial. However, two experimental studies^{1,2} have shown that this may also be inadvisable, although not quite so dangerous as overheating. In experimental burns in rats, the optimal environmental temperature range for survival seems to lie between 75 and 95°F.¹ Local refrigeration of an injured extremity may, on the other hand, be beneficial if ice is applied to the extremity during a prolonged crush³ or during the prolonged application of a tourniquet.⁴ It is obvious that more studies are required to determine the true value of local refrigeration in traumatic shock.

Stern,⁵ from Russia, offers evidence that secondary shock is benefited by the intracisternal injection of a solution of potassium phosphate. She claims that the potassium stimulates the sympathetic centers and that the phosphate by reducing the concentration of ionized calcium, depresses parasympathetic tone. Since sympathomimetic drugs are generally understood to be ineffective or harmful in shock, confirmation of this observation, especially with reference to the ultimate rates of survival, is desirable.

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MEDICAL EPONYM

HEERFORDT'S SYNDROME

In an article entitled "Über eine 'Febris uveoparotidea subchronica,' an der Glandula parotis und der Uvea des Auges lokalisiert und häufig mit Paresen cerebrosptinaler Nerven kompliziert [Febris Uveoparotidea Subchronica, Localized in the Parotid Gland and the Uvea of the Eye, and Frequently Complicated by Pareses of the Cerebrospinal Nerves]," in Albrecht von Graefes *Archiv für Ophthalmologie* (70:254-273, 1909), Dr. C. F. Heerfordt reports three cases. A portion of the translation follows:

The cases reported by me, together with that of Daireaux-Pechin and von Collomb's case constitute a clinically well-defined disease group with such peculiar characteristics that it would seem quite proper to establish them—for the present—as a special disease entity—a "febris uveoparotidea subchronica"—that is different from acute epidemic parotid fever.

We consider the following to be characteristic of this febris uveoparotidea subchronica: the protracted course of the illness, the prolonged low-grade fever, the localizations in the parotid gland and the uvea of the eye and, in addition, the frequent occurrence of complicating pareses of the cerebrospinal nerves. Finally, in my observation, this disease entity seems to be only mildly infectious.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

ATWOOD—CHARLES A. ATWOOD, M.D., of Taunton, died October 10. He was in his eighty-third year.

Dr. Atwood received his degree from Harvard Medical School in 1883. He was a member of the staff of the Morton Hospital and a consultant of the Taunton State Hospital. He had been medical examiner in the First Bristol District many years. He was a member of the Massachusetts Medical Society and the American Medical Association.

A brother survives.

CORRESPONDENCE

DEPRIVATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held October 6, the Board voted to revoke the license of Dr. Theodore Rosen, 9A Summit Avenue, Brookline, because of gross misconduct in the practice of his profession as shown by his conviction in court.

H. QUIMBY GALLUPE, M.D., Secretary
Board of Registration in Medicine

State House
Boston

BOOK REVIEW

Transurethral Prostatectomy. By Reed M. Nesbit, M.D. 4°, cloth, 192 pp., with 62 plates. Springfield, Illinois: Charles C Thomas, 1943. \$7.50.

This monograph is timely, and fills the need for an orderly description of transurethral resection. The material is arranged in four sections.

The first consists of ten chapters, which present the mechanics and principles of prostatic resection and comprise the most significant contribution of this monograph. Practical clinical information can be obtained from these clearly and well-written chapters. The excellent drawings by Mr. Didusch simplify and co-ordinate the various steps in the procedure.

The New England urologist will be interested in the second section (Chapter XI), which is an enthusiastic appraisal of the author's management of prostatism by transurethral surgery. The conservative resectionist who limits and selects his patients for transurethral surgery will note that this is a method not only for prostatic resection but also for transurethral prostatectomy, since the author does not hesitate to operate on glands yielding 100 to 150 gm. of tissue. He will read with envy and amazement that the technic offers the following advantages—freedom from postoperative discomfort and sepsis, bed confinement only for the day of operation, no postoperative strictures or urinary incontinence and a mortality rate as low as 1.2 per cent. Over a decade has passed since the introduction of the present methods of transurethral resection. With the comparative safety of modern surgery, the morbidity of a technic is almost as important as the mortality. This chapter occupies but 10 pages and, in the opinion of the reviewer, is entirely inadequate. It would be more convincing if a detailed and faithful follow-up study, including postoperative urologic and roentgenologic examinations, were a part of this chapter. Many urologists have subsequently operated on patients who had had transurethral surgery done by prominent resectionists, and it is surprising that such failures do not appear in the end-result statistics. It seems as though it were time for a definite evaluation of this procedure to be made.

The third section (Chapter XII) deals with the history of transurethral prostatic resection. It makes interesting reading and is well illustrated. The fourth is composed of a well-selected bibliography, grouped alphabetically according to the authors' names and also classified according to pertinent subdivisions.

This monograph is instructive but the reviewer does not believe that it will be instrumental in converting the conservative urologist to the author's point of view.

(Notices on page xii)

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CIVILIAN MEDICAL DEFENSE AND ITS ADAPTATION TO PEACETIME CIVIL LIFE*

A. WILLIAM REGGIO, Senior Surgeon (R), U.S.P.H.S.†

BOSTON

OUR normal way of living has been greatly upset, and we have gradually been adjusting ourselves to new conditions forced on us as a nation and as individuals as the result of a war not of our own choosing. We have been forced into a war by enemies who were quite sure that we, as a nation, could not get together in time to avoid defeat. They considered us selfish, stupid and soft because we lived at peace with our neighbors, respected the rights of others, and were unprepared to meet and repel their sneaking attack upon us. Perhaps we were a bit blind to the dangers threatening us, but somehow it is not in our make-up to attribute to any human being such low qualities as we have found our enemies to possess!

Be that as it may, we have swung into line in a manner characteristic of our way of doing things. Once we began, nothing was allowed to stand in the way of accomplishing the end toward which all our efforts were directed. That end is quite some way off as yet, but all of us and all our allies know that the ultimate end is victory for us. And—our enemies of the Axis know it, but do not as yet admit it—out loud!

The thought comes to mind, however, in all this hard struggle and increasing sacrifice, of what is going to happen when the final victory is won and we once again return to our peaceful manner of living. Shall we again lapse into our former error of assuming that all nations can be trusted to carry out their signed covenants? Are we going to forget the lessons we have learned the hard way? Are we going to allow the work done in setting up the medical organization of the Office of Civilian Defense to go to seed and fail to profit by it in the future just because peace has returned? I do not believe so—any

more than we should disband our police force just because no murder had been committed recently or there had been no riots for some time.

Before the Office of Civilian Defense was created, the only adequately organized disaster setup was the American Red Cross, but even it would have considerable difficulty in handling any sudden large-scale enemy action against us. This threat is spurring us on to get ready for the time when enemy action will strike this country, and should continue to drive us to perfect our civilian defenses. The threat has by no means been removed as yet, and may be even more imminent and nearer than we think. As the enemy becomes more desperate and despairing of the victory that they assumed to be certain for themselves, they may readily resort to action against our shores in an attempt to intimidate us and bolster their own failing morale. The work to perfect our civilian defense has been no small task, and the magnitude of it can be somewhat appreciated when one realizes that practically every community in the country has organized itself to ensure, in so far as possible, the care of injured people. Property when destroyed can be restored and rebuilt. Life cannot. Death is permanent.

In the Boston night-club disaster of some six months ago, it takes but little imagination to visualize what might have happened regarding loss of life if the civilian-defense organization had not been prepared to function. Although the deaths reached the distressing number of 491, it is safe to say that this number would have been larger but for the functioning of the Emergency Medical Service. Ambulances; doctors, nurses and hospitals were available and ready to handle the injured immediately after the disaster occurred. One thing above all stands out as instrumental in saving lives—the lack of it would quite definitely have created a most serious problem, but owing to the Emergency Medical Service it was instantly avail-

*Presented at the annual meeting of the New Hampshire Medical Society, Manchester, May 11, 1943.

†Regional medical officer, Office of Civilian Defense, instructor in surgery, Harvard Medical School, visiting surgeon, Massachusetts General Hospital.

able in abundance and to spare. I refer of course to blood plasma. At the time of the disaster over 2700 units of plasma set aside for the Emergency Medical Service were instantly available in the city itself, and a total of 3564 units in the State. It is doubtful whether such a supply would have been so quickly available under peacetime conditions. This plasma was on hand largely because of the tireless efforts of those whose job it was to think and plan for a catastrophe that might strike any community. This work is being carried on, and as of April 1 of this year, sixty hospitals in New England reported a total of 23,121 plasma units in storage and immediately available.

This is just one example of why we must not allow ourselves to relapse into blissful inertia when war conditions are no longer present and a general letdown would threaten the safety of any large number of people. How much plasma would have been available in the hospitals under the old conditions is, of course, a matter of speculation; but it is doubtful whether anywhere near an adequate number of units for a disaster of this magnitude would have been on hand, although a small number of units might have been obtainable from commercial sources.

What about the hospitals and the emergency organizations they have set up? Handicapped as these hospitals are by their greatly reduced staffs and personnel, they are, nevertheless, ready to function at a moment's notice should large numbers of casualties suddenly be brought to their doors. This has been no small task of organization in the face of continually dwindling medical and nursing staffs, as well as of the other personnel so necessary for the adequate functioning of any hospital. Being forced to run a hospital with about half its usual peacetime personnel is no easy job, to say nothing of the additional difficulties in trying to maintain and replace supplies of all kinds when they are becoming more and more difficult to obtain; and yet hospital administrators and superintendents are doing just these things.

The peacetime civilian hospital organized on an emergency wartime basis has already proved itself in a serious disaster not presumably of enemy origin. This same emergency that proved the worth and wisdom of a large store of plasma also showed the value of such civilian defense efforts in hospital organization.

It may not be generally known that during the Coconut Grove disaster 80 per cent of the casualties were brought into the emergency wards of two hospitals at the rate of one case in every eleven seconds. One hospital received 325 casualties, another 114. It needs no great stretch of the imagination to visualize what confusion might easily have resulted had not the Emergency Medical

Service been established, and through practice drills each person's role been set down and everyone made familiar with his specific duties. Short-handed as these hospitals were, there was no confusion; and it is quite certain that because of the well-devised plan and the well-drilled organization, not a single life was needlessly sacrificed or even jeopardized.

The reserve pool of nurses that had been organized for some time was called on, and the response on the part of these retired nurses to fill in for the emergency was more than adequate for the need. They came immediately and served without question, uncomplainingly and gladly. Many worked overtime for as long as there was any need for them. The Red Cross volunteer nurses' aides swung into line, responding in large numbers to fill any position requested. The entire Red Cross setup of ambulances and canteens worked steadily, in some instances day and night—long hours for many of them.

Why do I dwell at length on this particular disaster? It is for the purpose of bringing out the point that had it not been for the Emergency Medical Service the mortality would unquestionably have been much higher.

We are learning during these strenuous times how to function adequately with greatly reduced resources. We are building up a medical organization that will function on the instant, without becoming overwhelmed by a sudden wave of casualties in spite of fewer people to handle the situation. Through practice sessions the weak points are brought out, and these can be remedied at the next field exercise. We are learning to accomplish more, in spite of having less with which to work. We are learning the true value of many things to which we have in the past given but little thought because there was always plenty more where they came from. In plain language, we are learning the hard way to be less wasteful and more appreciative and conserving of what we have. We can already make less go farther, and much to our surprise find that it works rather well.

Another factor developed by the present threatening conditions is the arrangement for mutual aid between communities and states. It is quite possible that a state could be so seriously hit by disaster that it was beyond its own resources to cope with the conditions. The resources of neighboring states are now available and ready for such an eventuality, and they can send assistance quickly with little confusion, since their own emergency resources are well known and immediately available.

The work that has gone into the development and organization of medical resources should not

be lightly cast aside when peace returns. These services, possibly in a modified form, are a valuable adjunct in the event of any catastrophe involving human lives.

The question of an adequate number of nurses for the staffing of hospitals and for the taking care of patients in their homes is a serious one. "Luxury nursing," as it may be termed, is practically a thing of the past, and there is considerable difficulty in obtaining even essential and necessary nursing care. The replacement of nurses who have entered the armed forces is becoming increasingly difficult, since the number of new applicants for training for the nursing profession is not keeping up with the number of trained nurses being withdrawn. The reasons for this are many and readily understandable, but the solution of the problem is difficult.*

The establishment of pools from which nurses can be obtained when urgently needed is of much value. Many retired nurses are willing and glad to return to work, giving as many hours as they can. A number of these same nurses are taking refresher courses in nearby hospitals to brush up on such advances in nursing as have taken place since last they were in active practice.

Physicians, retired for some time, are back at work—especially in the hospitals—and having the time of their lives at it. The term "retiring age" under the present emergency conditions is no longer a compliment. Much valuable work is being done by the older men who so gladly return to work filling the vacancies caused by the younger ones who have gone into the service. All this wartime activity stimulates us to look ahead and to prepare our medical resources so that they will be ready to function when enemy action hits us and the care of casualties is imperative.

Why run the risk of throwing away all this tremendous effort just because the threat of enemy action against us will have been removed with the return of peace? Floods, hurricanes, conflagrations and catastrophes of one kind or another will continue at intervals even in peacetime. It would be little short of criminal to allow the preparations we have made for mutual aid in caring for those whom disaster will strike under war conditions to be dissipated and forgotten when peace returns. The effort necessary to keep a civilian-defense organization going in peacetime would of course be minimal, and the knowledge, coupled with a feeling of safety, that we were prepared to meet disaster in any form would more than repay the efforts of those people farsighted enough to hold such an organization together even if only on a small scale.

This trained and disciplined group would act with greater efficiency in aiding the already existing peacetime organizations than would people hurriedly gathered together, and would provide a reservoir of manpower that could be drawn on, with the knowledge that the needs of any particular situation could be met. By being ready they could make their work more effective. The practice gained will be invaluable if the enemy strikes, and inversely, experiences gained from enemy attacks will prove profitable in peacetime disasters. Co-operation and not regimentation has always been the American way. Mutual aid as exemplified by the civilian-defense organization is a typically American way of aiding our neighbors who are in distress. This may be in a local community, within a state or in another state—it makes no difference. The war has caused us to develop and perfect an organization for mutual aid unparalleled in our history. Without the Emergency Medical Service, untold numbers would needlessly suffer and die.

The value of all this is not conjectural. We have proof, not only in England but also in our own country, in the time when civilian-defense forces have aided materially in natural disasters caused by fire and flood. The aid rendered has been so valuable that it seems neither reasonable nor possible that a thinking people would be willing to give it all up when the present emergency is over.

My closing thought and appeal is to ask you all to consider seriously the possibility that the emergency medical services in your own communities will carry on and will preserve a type of organization that could be called up at any time to save life and property and alleviate the human misery that goes hand in hand with any disaster. An emergency, anticipated and prepared for, ceases to be an emergency. It is up to us to see to it that the lessons learned from the Emergency Medical Service are not thrown away.

17 Court Street

DISCUSSION

DR. C. H. PARSONS, Concord: Dr. Reggio's description of the value after the war of the services furnished by the Office of Civilian Defense is much to the point. However, they can be of value then only as they are adequately organized at the present time. The majority of our communities are extremely well organized. That has been proved in the several highly successful drills that have been held. The drills, however, have shown certain deficiencies, which have been due primarily to lack of attention to the details of organization and to inadequate practice.

During the summer, an attempt will be made by the state committee to aid each community in reorganizing

*At the time this paper was presented, the United States Cadet Nurse Corps program was not under way.

its medical services according to a plan that has been made necessary by the present types of bombing and by the new methods of medical care following thermal burns. This reorganization has been shown necessary by the events taking place during and after the Coconut Grove fire.

I am sure that the emergency medical services in the communities of New Hampshire will be adequately trained and organized to take care of any incident, should such an unhappy state of affairs occur.

DR. W. J. P. DYE, Wolfeboro: The question of civilian defense has been adequately and inspiringly covered by Dr. Reggio. A great many of us, particularly those in the smaller communities such as that from which I come, have a tendency to be optimistic about the situation. It looks as though things were rolling fairly well, and that the chances of any incidents in this country are quite small, so far as actual bombing or things of that sort are concerned; nevertheless, Dr. Reggio has men-

tioned that there is a possibility of nuisance bombing or some attempt to destroy civilian morale.

The entire civilian setup is, on the whole, so far as I can judge from my own and the neighboring communities, fairly well organized. A typical incident occurred in Wolfeboro not so long ago, when a large dairy farm suddenly caught fire in the early morning hours. It was in the middle of the winter, when the temperature was subzero, and the firemen worked under considerable difficulties. The motor corps and various other units were on the scene practically as soon as the firemen were, and they furnished hot coffee and gave first-aid care promptly and with a great deal of interest.

That was a small casualty in a small community. But if it is multiplied by many such casualties in large communities, such as are likely to happen in peacetime, and if we have, as Dr. Reggio has said, continued interest and continued practice in civilian-defense methods and in organization, then all these emergencies can be better met and we shall have achieved quite an advance in community and national service.

THE TREATMENT OF ANGINA PECTORIS*

A Summary of Ten Years' Objective Study

JOSEPH E. F. RISEMAN, M.D.†

BOSTON

IT IS well recognized that patients differ in their response to therapy, yet in evaluating the efficacy of treatment in angina pectoris this fact has not been taken into consideration. It is also self evident that various methods of therapy must differ considerably in value, yet there is little in the published reports or in the claims of the pharmaceutical houses to permit comparison.

Objective studies of the value of treatment in angina pectoris have been carried out in a special clinic of the Beth Israel Hospital since 1933. To date, sixty-eight different methods of chemical, physical and surgical therapy have been studied by clinical and objective procedures that permit unbiased comparison of effectiveness. Some of the results have been reported.¹⁻⁷ The detailed data of these and the unreported results are too voluminous to be presented in detail here, and will be the subject of a forthcoming monograph.

The purpose of this paper is to present a summary of these results, with special reference to variations in the response to therapy and to a practical plan of treatment with the methods most likely to be of value.

METHODS OF STUDY

The objective studies that have been carried out have been based on the following self-evident premises. First, since angina pectoris occurs only

in human beings, the value of therapy must be measured in terms of patients. Secondly, since exercise is the commonest precipitating cause of attacks, any treatment to be of value must enable the patient subsequently to do more work before experiencing pain. Observations during the last ten years have shown that the value of any form of treatment can be determined objectively by measuring the amount of work that can be done before angina is induced, provided that the measurements are made under conditions closely simulating those responsible for the majority of attacks in daily life, and that they are standardized in such a manner that the response to therapy is the only variable factor that can influence the exercise tolerance.

The standardized exercise-tolerance test. Previous studies¹ have shown that several factors materially influence the amount of work that can be done by patients with angina pectoris before pain is induced (Fig. 1‡). These factors have usually been overlooked by investigators studying the exercise tolerance of such patients. The importance of exercise in the cold must be emphasized, for if patients exercise at ordinary room temperatures, approximately one third fail to develop an attack,^{1, 8, 9} whereas in others the exercise tolerance varies independently of therapy. If these conditions are properly standardized, as shown in Fig.

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‡Figs. 1, 2, 4, 6 and 9 have been reproduced from the motion picture "Angina Pectoris," produced at the Beth Israel Hospital and based on these studies.

ure 2, the amount of work necessary to induce angina becomes remarkably constant (usually

sions of the clinical response to therapy were recorded, and also the number of attacks experienced

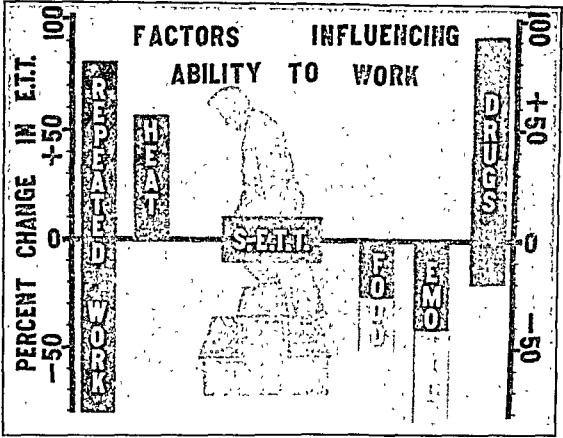


FIGURE 1.

around 10 per cent of the average exercise tolerance).

Method of administering medication for evaluating the response to therapy. The variable course of angina pectoris makes it necessary to evaluate

since the last visit. In addition, the standardized exercise tolerance was determined one or two hours after the last dose of medication.

Several months of observation were necessary to determine the usual frequency of attacks in daily

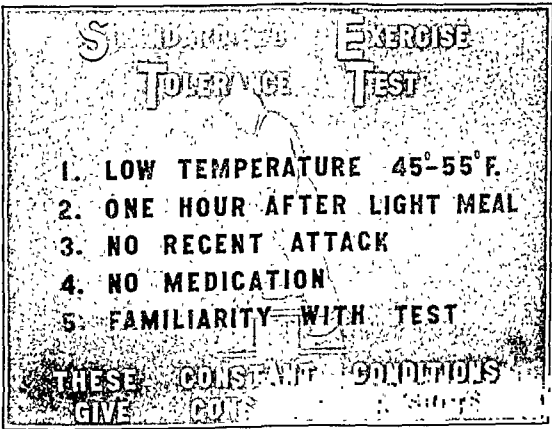


FIGURE 2.

the effect of therapy at frequent intervals. Patients were seen in a special clinic weekly. At each visit the patient's and the physician's impres-

life and the usual exercise tolerance. When these had been ascertained, medication was given three or four times daily for at least a week. If there

was no evidence of improvement, another therapeutic measure was tried. If there appeared to be a therapeutic response, a placebo resembling the drug being evaluated was given for one or two weeks or until the apparent therapeutic response disappeared. Later the studies were repeated or

Correlation between the results of the standardized exercise-tolerance test and the clinical response to therapy. The standardized exercise-tolerance test makes it possible to differentiate real improvement due to therapy and apparent improvement unrelated to it. Patients who show an in-

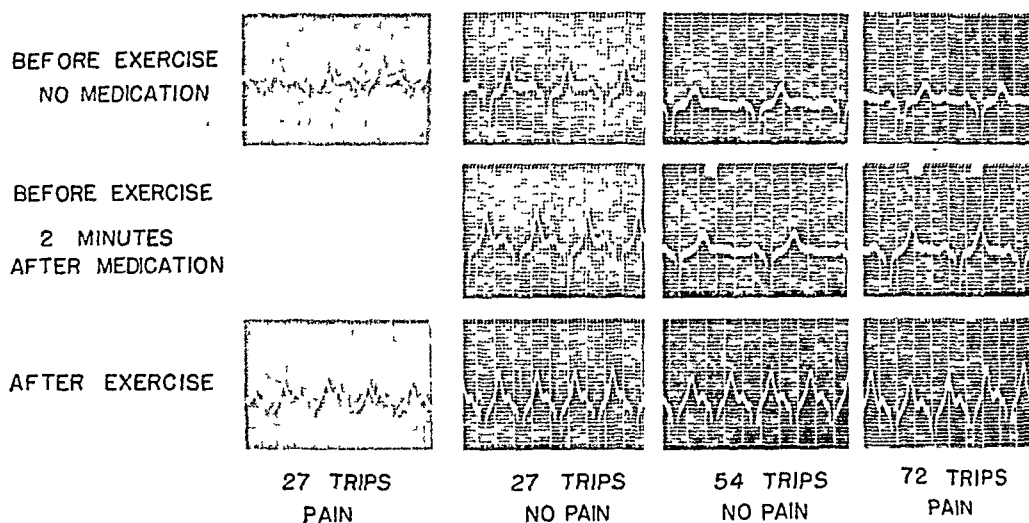


FIGURE 3. *Electrocardiograms before and after Exercise, without and with Medication (1/200 gr. nitroglycerin).*

at least two occasions, the medication being given in disguised form—painted with tincture of cudbear, sugar coated or enclosed in a capsule.

Electrocardiographic studies gave further objective evidence that the response to therapy was not psychologic or fortuitous but was due to a positive effect on the heart. In most patients with angina pectoris, exercise causes characteristic changes in the electrocardiogram that are commonest and most striking in the precordial lead.¹⁰ They consist of a deviation—usually a depression—of the initial portion of the RS-T segment. This begins shortly after the onset of exercise, reaches a maximum when the patient is forced to stop because of pain, and thereafter either subsides rapidly—frequently within fifteen seconds—or shows further progression, especially the height of the T waves. Because of the progressive and transient nature of the changes, the tracings must be obtained immediately after exercise, and only one lead can be observed during any one attack. The time necessary to adjust the electrodes and machine makes it impossible to obtain comparable tracings by any other technic.

Most therapeutic measures that decrease myocardial anoxia and thereby enable the patient to do more work without pain prevent or minimize the electrocardiographic changes that accompany exercise (Fig. 3).^{6,7} The degree to which these changes are prevented is an index of the therapeutic effect or potency of the medication and of the patient's response to it.

crease in exercise tolerance of 100 per cent or more following treatment usually have complete or almost complete freedom from attacks in daily life. An increase of 30 to 75 per cent is usually associated with a moderate diminution, but not complete disappearance of these attacks. An increase of 20 per cent or less is usually unassociated with any clinical improvement.

The converse is not true. Most patients with angina pectoris feel better after visiting the physician, regardless of the therapy prescribed. Furthermore, some of those with infrequent attacks have periods of relative comfort. Without an objective test, neither patient nor physician can say whether these periods of relief are the specific result of treatment or are merely coincidental with therapy.

Shortcomings of other methods used to evaluate therapy. The inadequacy of studying the efficacy of therapy by clinical evaluation alone is apparent from the above discussion. It is not surprising that the majority of published reports indicate that a wide variety of therapeutic agents—including many that are obviously inert—are apparently of value in treating patients with angina pectoris. It must be remembered that the clinical evaluation of the benefit of therapy is, in fact, the physician's impression of the patient's opinion of the response to treatment. Objective measurements are essential.

Attempts at having the patient report the response to therapy in terms of ability to perform

such customary tasks as walking and climbing stairs are similarly misleading. Few patients in variably experience pain in daily life after a given amount of work. Such factors as environmental temperature, food, emotion, physical activity and the relation to previous attacks cannot be readily

the results in 75 patients, chosen because they had been observed for long periods of time and because their response to many different forms of medication had been measured. All patients had Heberden's angina¹⁵ due to coronary-artery disease of arteriosclerotic origin. From 10 to 35 patients

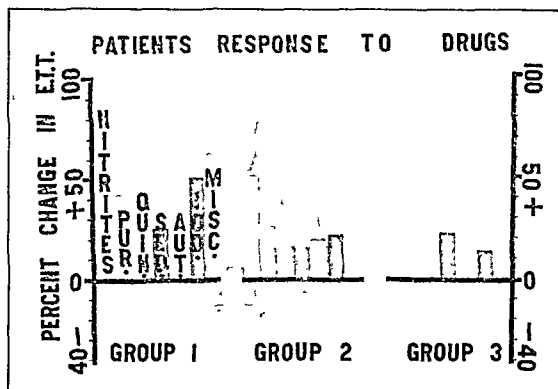


FIGURE 4.

This diagram shows the average of results in 3 patients in each of Groups 1, 2 and 3 who received nitroglycerin (nitrites), theobromine sodium acetate (purines), quimidine sulfate (quimidine), codeine sulfate (sedatives), atropine sulfate (autonomic drugs), enteric-coated potassium iodide (iodides) and locally applied heat (miscellaneous).

controlled or observed by the patient. Furthermore, such studies fail to reveal remissions in the course of the disease unrelated to therapy.

The electrocardiographic response to anoxia¹¹⁻¹³ is a valuable objective means of measuring the response to therapy, but has no close or clear-cut correlation to the clinical response. For example, nitroglycerin, the most potent drug available for the treatment of angina pectoris, does not yield such good results as does intravenous amino phyllin when measured by this method.¹² This is probably because the response to nitroglycerin occurs two or three minutes after its administration⁴ and may have ceased by the time that anoxia induces changes in the electrocardiogram. The response to cobra venom is an additional illustration of the inadequacy of using the electrocardiograph in evaluating clinical response. Since this drug causes no vasodilatation, the marked clinical improvement that may occur is not associated with any electrocardiographic improvement during exercise or induced anoxia.¹⁴

Subjects used in the present studies. For the purpose of this summary, an analysis was made of

were studied in evaluating most methods of therapy. The study of larger numbers was impractical, for the evaluation of any form of therapy requires weeks or months of study, and the clinical course of patients with angina pectoris is variable and is frequently interrupted by cardiovascular accidents and the like that are unrelated to therapy. These patients' clinical course and response to therapy were known so well, however, that an accurate biologic assay was possible. In the cases in which the therapeutic procedure was hazardous—surgery—or time consuming and expensive—bed rest, x-ray therapy and so forth—fewer patients were studied. In these cases the patients selected included one or two who were known to respond favorably to several simple methods of treatment, and also one or two who were known to respond to practically no method of treatment.

RESULTS

Variations in Therapeutic Response

It is possible to divide patients with angina pectoris into three groups on the basis of their

response to most therapeutic measures. Some patients, termed "marked reactors," show a striking response to practically all effective methods of therapy. Others, termed "moderate reactors," show a moderate response to the same therapeutic measures, and still others, termed "nonreactors," show little or no response to most available methods of therapy (Fig. 4).

The response to nitroglycerin can be used to determine the likelihood of response to other forms

of attacks in daily life. The average control deviation of the RS-T segment during pain was 2.43 mm., with a range of 1.5 to 3.5 mm., and after the same amount of work following nitroglycerin was 1.1 mm., with a range of 0.0 to 2.5 mm.

Group 3 (nonreactors). The remaining 40 per cent of patients showed no response to nitroglycerin and little response to most other methods of treatment. They showed the same elec-

TABLE 1. *Changes in the RS-T Segment of the Electrocardiogram during Exercise following the Administration of Nitroglycerin (1/200 gr.).*

GROUP NO.	PATIENT	BEFORE TREATMENT			TWO MINUTES AFTER TREATMENT		
		AMOUNT OF WORK NECESSARY TO INDUCE PAIN	OCCURRENCE OF PAIN	DEPRESSION OF S-T SEGMENT	AMOUNT OF WORK	OCCURRENCE OF PAIN	DEPRESSION OF S-T SEGMENT
		<i>trips</i>		<i>mm.</i>	<i>trips</i>		<i>mm.</i>
1	S. E.	27	Yes	2.7	27	No	0.2
	S. R.	51	Yes	2.7	51	No	0.5
	H. Schl.	54	Yes	2.5	54	No	0.4
	M. L.	40	Yes	1.8	40	No	0.0
	H. Schr.	22	Yes	1.5	22	No	0.0
	R. C.	26	Yes	1.0	26	No	0.0
2	P. R.	49	Yes	3.5	49	No	1.9
	L. W.	36	Yes	2.7	36	No	2.5
	B. L.	18	Yes	2.3	18	No	0.5
	S. W.	38	Yes	1.6	38	No	1.6
	S. L.	26	Yes	1.5	26	No	0.0
3	B. A.	50	Yes	4.0	50	Yes	3.0

of treatment and serves to divide patients into the three groups described, as shown in Table 1.

Group 1 (marked reactors). In this series 27 per cent of all patients fell in the first group. Two minutes after the sublingual administration of 1/100 gr. of nitroglycerin, these patients were able to perform approximately 100 per cent or more work than had been possible without medication. When given other drugs, they showed a definite increase in exercise tolerance—usually 50 to 100 per cent—and practically complete disappearance of attacks in daily life. The electrocardiogram before treatment and immediately following exercise sufficient to produce pain showed an average depression of the RS-T segment of 2.03 mm., with a range of 1.0 to 2.7 mm. Following the administration of nitroglycerin or other effective vasodilating measures, the average of the RS-T deviations after the same amount of work was 0.2 mm., with a range of 0.0 to 0.5 mm.

Group 2 (moderate reactors). Thirty-three per cent of all patients comprised the second group. They could do approximately 50 per cent more work after receiving nitroglycerin than before. When given other effective medication, most of them showed a moderate increase in exercise tolerance (25 to 50 per cent) and a definite decrease but not complete disappearance

trocardiographic changes during exercise whether therapy had been given or omitted.

Group 3 contained a high percentage of women and a low percentage of thin persons and of patients whose illness began before the age of fifty. Hypertension was somewhat commoner in Group 3 than in Group 1, and there was a high percentage of patients with low exercise-tolerance tests. Striking exceptions were frequent, however, and in any given case no characteristics other than the response to therapy served to differentiate the groups. In particular, the frequency and severity of attacks and the frequency of cardiac hypertrophy or abnormalities of the electrocardiogram at rest were approximately the same in all three groups.

There was a striking difference in the mortality of the groups (Fig. 5). During the period of observation, death occurred in 15 per cent of the patients in Group 1, 28 per cent in Group 2 and 43 per cent in Group 3. Conversely, after ten years of illness, 30 per cent of the patients in Group 1 were still living as compared with 16 per cent in Group 2 and 3 per cent in Group 3. Viewed in the light of the pathological studies of Schlesinger, Blumgart and their associates,¹⁶⁻¹⁸ this suggests that the patients in Group 3 represent those in whom the collateral circulation has compensated to the maximum extent. The coronary circulation

of such patients has little reserve, so that neither an increase in blood flow due to the use of vasodilators nor the development of additional anastomotic channels following additional coronary

crease in the standardized exercise tolerance and a corresponding decrease in the frequency of attacks in daily life usually occur, especially in Group 1 patients. This clinical improvement is

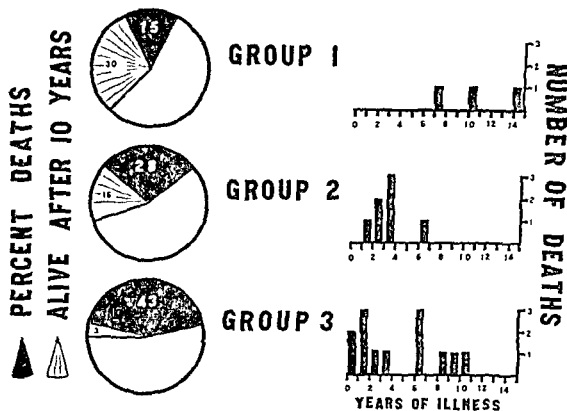


FIGURE 5. Mortality in Patients with Angina Pectoris.

occlusion is possible. Patients such as those in Group 1, on the other hand, have developed a well-functioning system of anastomotic channels with considerable reserve, so that an increase in blood flow occurs with vasodilating drugs and additional collaterals develop following coronary occlusion.

During the course of observation, several patients showed a change in ability to respond to therapy. Five patients who originally responded strikingly (Group 1) later responded to a lesser degree (Group 2). A sixth became completely unresponsive to medication for several months (Group 3) and died. Similarly, 2 patients originally in Group 2 suddenly failed to respond (Group 3), and 1 died within a few months after this change. On the other hand, 4 patients originally in Group 3 improved during the period of observation; 2 were ultimately classified in Group 1 and the other 2 in Group 2. In at least 2 of these patients, the improvement occurred after recovery from an episode of myocardial infarction.

Comparative Value of Therapeutic Measures

The comparative value of sixty-eight different therapeutic agents can be separated into three groups—those of marked value, those of moderate value and those of no value—on the basis of clinical effectiveness, low toxicity and low cost (Table 2).

Clinical effectiveness. When a therapeutic agent is given in adequate doses, a definite in-

crease in the standardized exercise tolerance and a corresponding decrease in the frequency of attacks in daily life usually occur, especially in Group 1 patients. This clinical improvement is

usually accompanied by a decrease in the electrocardiographic changes following exercise.

Low toxicity. This includes not only freedom from untoward reactions but also ease and practicability of administration in clinical practice.

Low cost. The importance of cost to the patient lies in the fact that angina pectoris and its underlying coronary arteriosclerosis are chronic conditions and that treatment must be continued over a long period, usually for life. To be of practical value, therefore, therapy must be sufficiently inexpensive so that the patient will be able to continue treatment for as long as necessary. The marked difference in cost of various commercial preparations without regard to their clinical effectiveness has been illustrated.⁸

The therapeutic agents of marked value were of three types as measured by results. The majority of agents resulted in an increase in exercise tolerance of 30 to 100 per cent or more in at least half the patients in Group 1. A few agents—the sedatives, atropine and potassium iodide in large doses—were not of such striking value, but were of appreciable benefit to some patients in Group 3 for whom few other satisfactory agents were available. The surgical procedures—total thyroidectomy and alcohol injection—were included because although costly, difficult to perform and not infrequently accompanied by untoward effects.

TABLE 2 *Comparative Value of Methods of Treatment.*

TYPE OF THERAPY	DEGREE OF VALUE		
	MARKED	MODERATE	NONE
Nitrites	Nitroglycerin, 1/100 gr Nitroglycerin, 1/500 gr Octyl nitrite Amyl nitrite	Erythrol tetranitrate, ¼ gr, 4 times daily Mannitol hexanitrate, 1 gr 4 times daily	Sodium nitrite, 1 gr, 4 times daily
Purines	Theobromine and sodium acetate uncoated, 7½ gr, 4 times daily Theophylline and sodium acetate, uncoated, 3 gr, 4 times daily Theophylline and calcium salicylate (Phylloin), 8 gr, 4 times daily Theobromine sodium acetate, enteric coated, 7½ gr, 4 times daily Aminophylline, 3 gr 4 times daily Theophylline methyl glucamine (Glucophyllin), 4 7/10 gr, 4 times daily	Theophylline, 4 gr, 4 times daily Theobromine, 5 gr, 4 times daily Theobromine and sodium salicylate (Diuretin), 7½ gr, 4 times daily Theobromine and calcium salicylate (Theocalcin), 15 gr, 4 times daily Theophylline diethanolamine (Deriphyllin), 1 cc, 4 times daily Theophylline monoethanolamine (Theamin), 3 gr, 4 times daily	Caffeine citrate, 2 gr, 4 times daily Theobromine and calcium gluconate (Calpurite), 15 gr, 4 times daily
Sedatives	Phenobarbital, ½ gr, 4 times daily Codeine sulfate, ½ gr, 4 times daily Cobra venom, intramuscularly	Theamin with amytal 3¼ gr, 4 times daily Theominol, 5/8 gr, 4 times daily Dilaudid, 1/20 gr, 4 times daily Bed rest for 6 weeks	Papaverin, ½ gr intravenously
Cinchona derivatives	Quinidine sulfate, 5 gr, 4 times daily Quinophylline (quinidine sulfate, 5 gr, and aminophylline, 3 gr), 4 times daily	Quinine sulfate 5 gr, 4 times daily	
Procedures or drugs acting on the autonomic nervous system	Pressure on the carotid sinus Atropine sulfate, 1/120 gr, 4 times daily	Physostigmine salicylate, 1/40 gr, 4 times daily Amphetamine (Benzedrine) sulfate, 1/12 gr, 4 times daily	X radiation of adrenal glands X radiation of thoracic sympathetic nerves Novatropine, 1/12 gr, 4 times daily Syntropan, 1½ gr, 4 times daily
Iodides and intravenous saline solution	Potassium iodide 1 gm enteric-coated tablets, 3 or 4 times daily	Normal saline solution, 500 cc intravenously, daily Sodium chloride, 5% solution, 200 cc intravenously, daily Sodium iodide 5% solution, 200 cc intravenously, daily	Potassium iodide, saturated solution, 15 drops 3 times daily Lugol's solution, 15 drops 3 times daily
Surgical	Total thyroidectomy Paravertebral injection of alcohol		Denervation of thyroid gland
Miscellaneous	Heat	Inhalation of oxygen during exercise Whiskey 1 oz before work Metrazol, 3 gr, 4 times daily Inhalation of trichlorethylene	Lactose Sodium bicarbonate 5 gr 4 times daily Calcium salicylate, 5 gr 4 times daily Ethylene diamine hydrochloride 1 gr 4 times daily Coramine 1 teaspoonful 4 times daily Mvorol, 2 tablets 4 times daily Depropinex, 2 cc, daily Dinitrophenol, 25 mg 4 times daily Cigarette smoking Estrogenic substances 10 000 I U, daily Testosterone 25 mg, daily Thuramine 10 mg, 4 times daily Niacin, 50 mg, 4 times daily Kerr abdominal belt Digitalis Theophyllinated genin of squills*

they were nevertheless of striking value in a few patients not helped by other and simpler means.

The therapeutic agents of *moderate value* were those the administration of which was followed by some improvement but not of sufficient degree or frequency to recommend them for routine use, —especially since more valuable methods of thera-

py is somewhat less valuable and is also more expensive. In using the enteric-coated preparations, it must be understood that several hours will elapse before they become effective (Fig. 7). It is important, therefore, to administer medication before the patient retires, for it is this dose that is effective on the following morning. In many cases it

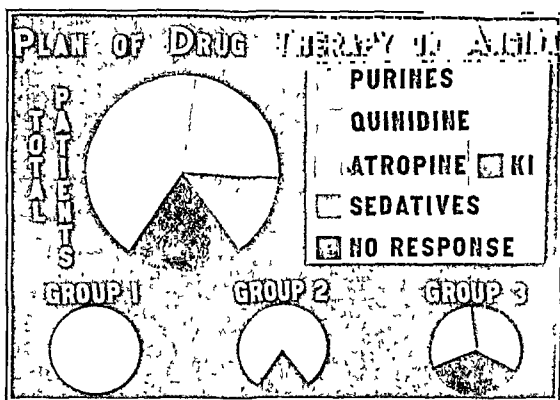


FIGURE 6.

py were available, —and those, such as oxygen therapy, that were clinically effective but were impractical for clinical use.

The therapeutic agents of *no value* resulted in no appreciable increase in standardized exercise tolerance. Any clinical improvement that followed their use could be ascribed to psychologic influence.

ROUTINE TREATMENT

Treatment should be individualized. Careful questioning and prolonged observation may reveal specific precipitating factors — such as walking uphill or after meals, going out into the cold or emotional disturbances — that can be guarded against or eliminated. A change in habits, the use of sedatives or the prophylactic use of nitroglycerin at appropriate times is frequently of value in such cases. In a few cases (less than 1 per cent) hyperthyroidism, anemia, polycythemia or arrhythmias responsible for attacks may be discovered and corrected.

Medication is usually necessary. The purines are most likely to be of value (Fig. 6). Theobromine and sodium acetate, enteric-coated (7½ gr., four times daily), is the drug of choice. Theophylline and sodium acetate (3 gr.) and theophylline and calcium salicylate (8 gr.) are equally helpful but more costly. Aminophylline (3 gr.)

is advisable to give in addition a single dose of nonenteric-coated medication on the patient's arising. The purines were of benefit in 43 per cent of all patients (88 per cent in Group 1, 50 per cent in Group 2 and 12 per cent in Group 3).

In addition, especially during the first few weeks of therapy or if the symptoms are severe, it may be advisable to give 1/400 gr. of nitroglycerin under the tongue every hour when the patient is awake. Sedatives may be given as an adjunct. Although the latter may not increase the exercise tolerance to a striking degree, they help to stabilize the patient emotionally and make the pain easier to bear.

If this regime is of value, it will be evidenced within a week by the complete or almost complete disappearance of attacks in daily life. Any improvement short of this is probably not due to the medication used.

If no satisfactory response is obtained, it is advisable to substitute quinidine sulfate (5 gr. three or four times daily) as the drug next most likely to bestow benefit. Quinidine is about as effective as the purines, and the toxicity in patients with angina pectoris and normal cardiac rhythm is low. Sixty-one per cent of all patients were benefited by the purines or quinidine (all those in Group 1, 50 per cent in Group 2 and 24 per cent in Group 3).

The treatment of the remaining two fifths (39 per cent) of patients, especially those in Group 3, is a difficult problem, and future research should be directed toward the care of this group. Atro-

If the symptoms reappear when the patient returns to normal activity, cobra venom is worthy of a trial.^{14, 20} This drug diminishes attacks without affecting the underlying cardiac mechanism

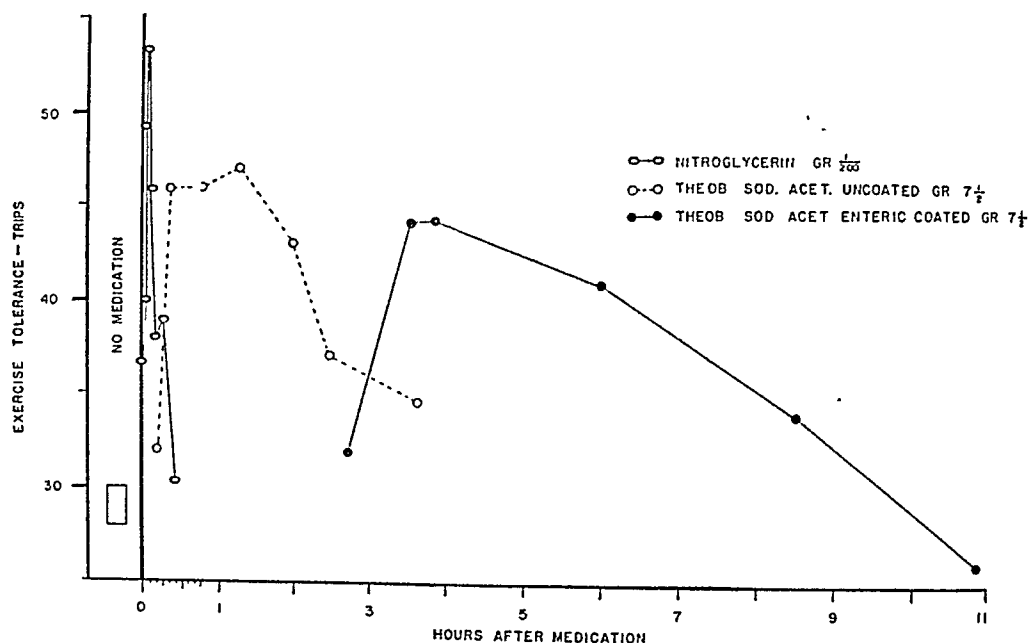


FIGURE 7. Comparative Effect of Nitroglycerin and Theobromine Sodium Acetate, Both Uncoated and Enteric-Coated, in Patient S. W. (Group 2).

pine sulfate (1/120 gr., four times a day) was of some value in approximately 10 per cent of such patients in Group 2 and 6 per cent in Group 3. Potassium iodide in comparatively large doses (1.0 gr. in an enteric-coated tablet, three or four times daily)¹⁰ was of value in an additional 12 per cent in Group 3. The sedatives, especially codeine sulfate, helped another 20 per cent in Group 3. There remain about 20 per cent of all patients (two thirds of whom were in Group 3) who responded to none of these medications.

TREATMENT OF SEVERE ANGINA PECTORIS

In many cases, especially in patients with severe angina pectoris who fail to respond to this regime, it is advisable to use a combination of therapeutic agents. While admittedly a "shotgun" method, the results obtained in such patients and the absence of other simple effective therapeutic measures justify its use.

Such patients should have a period of complete bed rest combined with adequate sedatives and small hourly doses of nitroglycerin. In some cases it is advisable to give in addition adequate doses of an active purine and, if necessary, quinidine sulfate. This regime usually results in the complete disappearance of pain within a week, unless there has been a recent coronary occlusion or unless a strong emotional element is present.

responsible for the pain. It must be given by injection, daily for at least a week and two or three times weekly thereafter.¹⁴ Despite these drawbacks, cobra venom, in certain cases, obviates the necessity for surgery.

Only if these measures fail to give relief should surgery be considered. Few patients, however, come to surgery (Fig. 8). At the Beth Israel Hospital, in 46 per cent of the patients with angina pectoris the disease was so mild even without therapy that surgery was unnecessary. In an additional 24 per cent, the response to medicinal therapy (exclusive of cobra venom) made surgery unnecessary. Of the remaining 30 per cent, approximately half were unsuitable surgical risks, and half the remainder refused operation when the risk and the likelihood of benefit were explained. As a result, surgery was performed in approximately 7 per cent of patients with angina pectoris.

In our experience, total thyroidectomy^{21, 22} has given more striking results than has any other form of therapy (Fig. 9). It is the surgical procedure of choice in patients with normal basal metabolic rates, prolonged but nonprogressive symptoms and a fair life expectancy who are adequate surgical risks. Suitable cases are admittedly few, but thyroidectomy may be a valuable means of alleviating symptoms and restoring physical ac-

tivity in those few to whom there is little else to offer.

Some form of surgery of the sympathetic nervous system may be employed in patients not suit-

Experience has shown that the above plan goes a long way toward prevention of attacks of angina pectoris. It has enabled many patients to increase their physical activity and in some cases to return

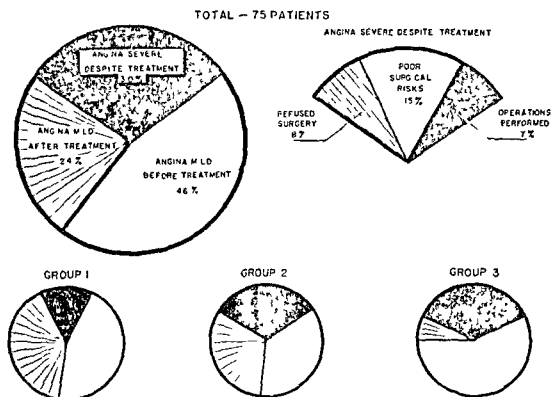


FIGURE 8. The Frequency of Surgical Treatment in Angina Pectoris

able for total thyroidectomy. Alcohol injection is at present considered to be the method of choice, but it rarely results in any increase in ex-

ercise tolerance and may be followed by a neuritis.²³⁻²⁶ The comparative freedom from pain that occurs in some patients, however, justifies the use of this method in the few selected patients who may require such relief.

to gainful occupation. Information concerning prolongation of life is difficult to obtain, but it is logical to reason that freedom from attacks in-

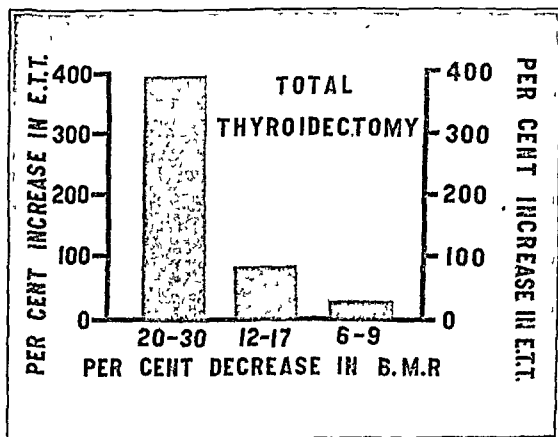


FIGURE 9.

ercise tolerance and may be followed by a neuritis.²³⁻²⁶ The comparative freedom from pain that occurs in some patients, however, justifies the use of this method in the few selected patients who may require such relief.

indicates comparative freedom from the physiologic mechanism responsible for some of the complications.

SUMMARY

An objective evaluation of the efficacy of treat-

ment of angina pectoris carried out over a ten-year period shows that 27 per cent of patients respond strikingly to practically all available forms of therapy, 33 per cent respond to a moderate degree, and 40 per cent usually fail to respond appreciably. This variation in therapeutic response should be taken into account in any study of the efficacy of treatment of angina pectoris.

The clinical evaluation of the efficacy of therapy is extremely difficult and unreliable. Nothing short of complete or almost complete disappearance of attacks can be considered as a favorable response, and it must be remembered that such periods may be spontaneous and not related to treatment.

Of the sixty-eight methods of therapy evaluated, twenty were found to be of considerable value, twenty-two were of slight value, and twenty-six were of psychologic value only.

In prescribing medicinal therapy, the drugs of choice are nitroglycerin (1/400 gr. every hour), theobromine and sodium acetate (7½ gr., four times daily), quinidine sulfate (3 to 5 gr., four times daily), atropine sulfate (1/150 gr., four times daily), enteric-coated potassium iodide (1.0 gm., four times daily), cobra venom (given intramuscularly) and the sedatives. The plan of treatment outlined was of value in approximately 80 per cent of all patients.

Few patients require surgery. Total thyroidectomy is of considerable value for selected patients. The paravertebral injection of alcohol gives symptomatic relief to others.

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CLINICAL NOTE

LARYNGOPYOCELE

REPORT OF A CASE

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A LARYNGOCELE or aerocele is supposed to be a congenital sac due to a prolongation of the ventricle of Morgagni. It is normal in certain groups of monkeys and is then bilateral. It is

tracheal rings seemed normal. The right cord was red and indistinct and was partly obscured by a red and protruding false cord. There was some limitation of motion on the right side, as well as marked fullness on the outside of the neck just to the right of the larynx. The roentgenologist (Dr. A. S. MacMillan) reported an aerocele of the right ventricle (Fig. 1).

At operation, an oval sac measuring 2 by 3 cm. was located at the right of the thyroid cartilage, extending up to the cornu of the hyoid bone and reaching posteriorly and laterally to the region of the superior laryngeal nerve. Its wall was thin and slightly adherent at the fundus. The other end of the sac took the form of a neck that penetrated the thyrohyoid membrane and curved over the superior border of the thyroid cartilage, passing down its inner surface and under the right false cord to its

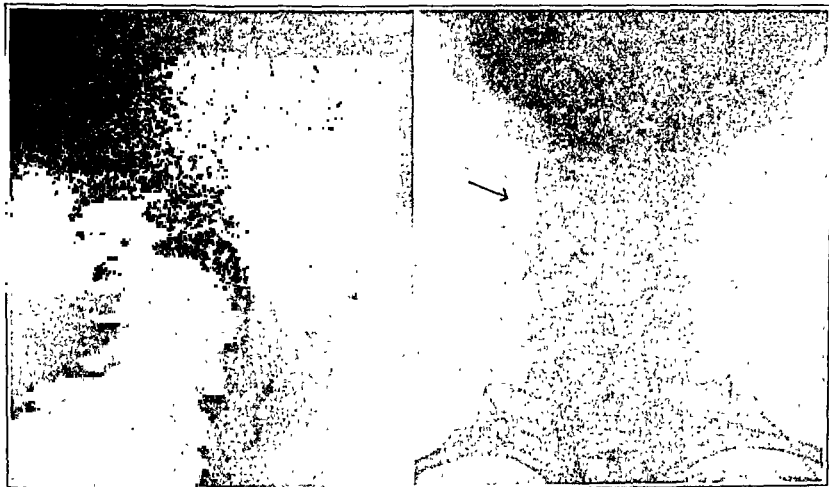


FIGURE 1. X-Ray Films Taken in the Lateral and Anteroposterior Positions.

sometimes referred to as a "monkey pouch." The literature contains reports of about 80 cases in human beings, by far the greatest proportion being found at autopsy or in dissecting rooms. The presence of pus in the laryngocoele is rare, and in the case reported below may have taken place at the time of the patient's extremely "sore throat" a year and a half previous to examination.

CASE REPORT

A 45-year-old woman, referred by Dr. W. W. Marston of Newton, had complained of hoarseness intermittently for 1½ years. She had received a satisfactory tonsillectomy 25 years previously. She had had a very sore throat 1½ years previously.

Examination of the larynx showed that the left cord was normal in color and motion. The epiglottis and

origin in the ventricle of Morgagni. The sac was removed after suturing and severing the neck. It was filled with a fluid pus, thus making it a pyoceles and not an aerocele. A stained smear of the pus showed gram-positive bacilli, and a culture was negative for beta-hemolytic streptococci. The pathologist's report was as follows: "The specimen consists of a small oval cystic structure opened at one end and measuring 3.5 by 2.0 by 1.0 cm. Its outer surface is roughened from resection. The wall is fibrous and less than 1 mm. in thickness. The lumen is empty, and the lining is smooth and pinkish gray. Microscopically, the cyst-like cavity is lined by ciliated columnar epithelium, supported by stroma that is rich in lymphocytes and at one point shows a nest of mucous glands. Diagnosis: laryngocoeles?"

The patient made an uninterrupted convalescence. After 2 weeks the wound was healed, the hoarseness had disappeared, and the appearance and motion of the larynx had become normal.

Those seeking further information on this rare condition are referred to an excellent article by

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Freedman,¹ published in 1938. He outlines the history of the discovery of the laryngeal ventricles, sometimes called the ventricles of Morgagni because of the latter's detailed description given in 1741. Freedman refers to the fine dissections made of this space by Hilton² in 1837 and to the discovery of the sacculus laryngis, which contains many mucous glands; he ventures the theory that these glands furnish the fluid to lubricate the vocal cords. He then elaborates on the physiology of this function of the sacculus, and on the consequences of its failure. The sacculus or its extension, he says, represents the air sac of the anthropoid apes. Freedman expounds the theory that apes and other climbing mammals are at times forced to cease breathing temporarily, and that these air sacs are filled with oxygen on inspiration but with carbon dioxide during expiration, and therefore act as mixing chambers. He reports a case of pyocele in a fifty-four-year-old

man and describes his operative technic. He also cites a case of prolapse of the sacculus and a laryngocele in a nine-week-old boy. His article ends with references to ten other articles.

Jackson and Jackson,³ in their textbook published in 1937, state that laryngocele is a very rare disease and that they have seen only 2 cases. In both these cases the sac protruded into the lumen of the larynx and not into the neck, and contained air and not pus as in the case here reported.

SUMMARY

A case of laryngopyocele is reported, and the pertinent literature is discussed.

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MEDICAL PROGRESS

PANCREATIC INSUFFICIENCY AND THE CELIAC SYNDROME (Concluded)

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PANCREATIC-ENZYME ANALYSIS

THE frequent familial history, the apparently congenital nature of the process, the early onset of symptoms and the presence sooner or later of pulmonary infection assist in the clinical differentiation of pancreatic insufficiency from idiopathic celiac disease. Measurement of the activity of pancreatic enzymes in the duodenal content, however, appears to be the most valuable single laboratory aid in making this differentiation and in establishing the diagnosis in the absence of symptoms of the celiac syndrome. Two recent extensive studies of pancreatic-enzyme activity in infants and children, with particular reference to the celiac syndrome, have been made. Andersen²⁶ included data on such activity in the duodenal content of 15 patients who had a clinical history consistent with the diagnosis of pancreatic fibrosis, in a report of enzyme studies on 98 infants and children including some with chronic diarrhea, others with extreme marasmus and some with a classic picture of true celiac disease. Farber, Maddock and Shwach-

man²⁵ presented data on the pancreatic-enzyme activity of 150 infants and children including normal patients with chronic nutritional failure, 11 with true celiac disease and 22 with pancreatic fibrosis. The results of these studies, in agreement with all similar observations, such as those by Siwe,²⁷ Benoit,²⁸ Tiling²⁹ and others³⁰ who have studied pancreatic enzyme activity in the celiac syndrome in small numbers of patients, demonstrated that markedly diminished or absent activity of pancreatic enzymes in the duodenal content, particularly that of trypsin and lipase, characterizes all cases of pancreatic fibrosis, in contrast to the essentially normal values found in patients with true celiac disease and other types of chronic failure of nutrition. An important pancreatic lesion was found at autopsy in every patient in whom pancreatic achylia had been demonstrated during life. Farber, Maddock and Shwachman state that patients with sprue, idiopathic steatorrhea or that form of the celiac syndrome associated with malrotation of the bowel have normal pancreatic enzyme activity and do not differ in this respect from patients with true celiac disease. The duodenal content in patients with pancreatic fibrosis is frequently so striking in its scantiness and viscid-

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C Thomas, 1942. \$5.00).

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ty that diagnosis may be made with considerable accuracy on gross inspection alone. All patients with chronic nutritional failure may be divided provisionally into two large groups on the basis of pancreatic enzyme analysis: those with normal activity and those with markedly reduced or absent activity. From this temporary classification further subdivision may be carried out in the group with normal enzyme activity. The generalization has been made that the diagnosis of true celiac disease, idiopathic steatorrhea, nontropical sprue, pancreatic fibrosis or other similar conditions should not be considered as established until the pancreatic-enzyme activity in the duodenal drainage has been measured.

Andersen²⁶ has recognized two groups of patients who may be separated from those with celiac disease and with pancreatic fibrosis on the basis of enzyme analysis. She found some patients with what she called "near-celiac" disease who showed intolerance to starch in the diet, a low level of amylase in the duodenal juice, and starch in the stools but no excessive stool fat. Such patients have a relatively mild, though prolonged, clinical course. In the second group she placed those with idiopathic steatorrhea, intolerance to fat, a high concentration of stool fat, normal amounts of pancreatic enzymes and a severe and protracted clinical course. She suggests that in these patients the difficulty lies in the absorption rather than in the digestion of fat. In 3 patients with severe marasmus she found depression of activity of trypsin, amylase and lipase, with a return to normal after clinical improvement. Farber, Maddock and Shwachman²⁵ encountered patients with failure of nutrition in whom selective lipase deficiency was demonstrable in the presence of normal amounts of trypsin and amylase. They reported also the demonstration of absence of trypsin activity in an infant with meconium ileus.

Andersen²⁶ has suggested that the assay of trypsin alone is a reliable means of diagnosis of pancreatic deficiency. In general, she states that few errors in the diagnosis of pancreatic fibrosis will be made if amylase and lipase are not measured. Rare exceptions may be encountered, such as a case of selective trypsin deficiency in a boy with chronic nutritional failure that did not resemble the celiac syndrome; in the duodenal content normal amylolytic and lipolytic activity was demonstrated.²⁵ Particularly during the first few months of life, the assay of amylase yields little information of value, since this enzyme is present in such low concentration in normal infants.²¹ In many older infants and young children with chronic diarrhea amylolytic activity in the duodenal content may be reduced.²⁶

It appears probable that further anomalies of pancreatic exocrine function will be discovered when studies of pancreatic activity are carried out on large series of infants and children. In patients with pancreatic fibrosis Maddock, Farber and Shwachman²² found that stimulation of the pancreas by secretion had little effect on the duodenal content and was not essential for the correct interpretation of the enzyme activity in the pancreatic juice. Stimulation by secretion, however, causes a moderate increase in amylolytic activity in patients with true celiac disease and a marked rise in those with chronic nutritional disturbances of the nonceliac type.²²

Pancreatic achylia appears to be a permanent finding unaffected by pancreatic substitution therapy or any other form of treatment, since six determinations of enzyme activity in the duodenal content of a patient made between the ages of five and twenty-five months showed no appreciable change in the level of enzyme activity, although the patient's general condition appeared to improve.²⁵

Detailed descriptions of methods of pancreatic-enzyme analysis for use on infants and children have been given.^{20, 23, 24} It appears clear that this field of investigation, opened by the pioneer work of Hess³⁵ on infants in 1912, will have much value. The use of Mecholyl and secretin in studies of pancreatic function should yield data of great interest.³⁶

METABOLIC STUDIES

Shohl, May and Shwachman²⁷ found the weight of the feces of patients with pancreatic fibrosis to be greater than that in any other condition in childhood. In a series of metabolic studies designed to furnish data concerning altered nitrogen metabolism in pancreatic fibrosis under controlled conditions, when native protein was removed from the diet, there was no difference in the weight of the feces. When both protein and fat were omitted, however, and nutriment was given parenterally, the residue of the feces was small. Pancreatic substitution therapy was followed by reduction in the weight of the feces, but not to the normal level. Those writers concluded that the amounts of nitrogen in the feces of patients with pancreatic fibrosis may exceed that in the urine and reach three or four times that in the feces of normal infants. Excessive nitrogen in the feces is the cause of a negative nitrogen balance and is partly responsible for the loss of weight and the deterioration of patients with this disease. With respect to high fat in the stools, excessive excretion of nitrogen in the feces and marked increase in the weight of the stools, children with pancreatic

fibrosis behave as do dogs in which the pancreatic juices have been excluded from the intestines. Shohl et al. were able to reduce the amount of fecal excretion and nitrogen excretion in the feces to normal limits when a fat-free ration, consisting of casein hydrolysate and glucose, was administered.

It may be of interest to mention the similar results of metabolic studies in 4 adults with pancreatic achylia reported by Beazell, Schmidt and Ivy.³⁸ Although the etiologic factors were unknown, the diagnosis was made on the basis of an absence of pancreatic enzymes in the duodenal drainage, an increase in the quantity of nitrogen and fat in the feces and a reduction in the wastage of both nitrogen and fat with substitution therapy. The patients were placed on a standard balanced diet supplying 64 gm. of protein and 112 gm. of fat daily for a period of six days. Beginning with breakfast on the fourth day, the patients were given with each meal 8 gm. of pancreatin in the form of enteric-coated tablets. A total of 24 gm. was given daily, one half immediately before and one half immediately after the meal. The 24 gm. corresponds to approximately 240 cc. of pancreatic juice, which represents only 15 per cent of the quantity normally estimated to be secreted by adults within twenty-four hours. After one month on this dose, the daily dose was progressively reduced until only 2 or 3 gm. was given with each meal. Response was noted by observing the subjective reaction, the character of the stools, the reduction in the frequency of stools, the gain in weight and the increased strength. These authors state that they have never seen pancreatic achylia, either clinically or in an experimental animal, that failed to respond to adequate enzyme therapy. Conversely, in the absence of demonstrable pancreatic insufficiency enzyme therapy never effected reduction in the nitrogen or fat of the stool.

Although steatorrhea has been stressed as one of the most characteristic findings in both pancreatic fibrosis and celiac disease, to the extent of including the word in the name of the disease,¹³ wide variations in the amount and kind of fat in the stool may be encountered. It should be recalled that the fat content of stool specimens of normal infants and children varies from 10 to 80 per cent of the dried feces.³⁹ Andersen⁴⁰ found that it increased to 30 to 80 per cent of the dry weight when the patient was given a whole-milk formula or an average mixed diet. Only 7 of the 35 patients with pancreatic fibrosis proved at autopsy studied by Blackfan and May¹⁵ had stools that were described as fatty. Examination of the stools of patients with pancreatic fibrosis for the ratio of neutral fat to hydrolyzed fat⁴¹ has not

served to differentiate this disease from celiac disease, since fat may normally be split by intestinal lipase in the absence of pancreatic lipase.⁴²

In the entire group of celiac diseases, absorption of fat is disturbed, although the mechanism may differ from case to case. Measurement of the absorption of vitamin A from the intestines was proposed by Breese and McCoord⁴³ as a test to aid in the diagnosis of celiac disease. The studies of May and McCreary⁴⁴ show that a low rise in the vitamin A absorption test is found in both celiac disease and pancreatic fibrosis. Differences in the degree of decreased absorption of vitamin A are detectable, but are not great enough to be of aid in differentiating these two conditions in a given patient. May and McCreary found no improvement in true celiac disease in the absorption of vitamin A when the vitamin was introduced intraduodenally and active intestinal peristalsis was maintained with Mecholyl.

An observation of considerable importance concerning the increased absorption of vitamin A in pancreatic fibrosis when the motility of the bowel is increased has been described by Flax, Barnes and Reichert.³⁰ Proceeding on the assumption that the inefficient absorption of vitamin A as well as of glucose is probably associated with the lack of tone and abnormal motility of the intestinal tract, they administered Prostigmine parenterally to a patient with pancreatic fibrosis and observed an almost immediate rise in the blood level of vitamin A. They chose this drug because of its success in restoring muscle tone in postoperative ileus.⁴⁵ After a period of five months, during which Prostigmine Bromide was given in amounts of 7.5 mg. three times a day, the absorption of vitamin A showed a normal curve. A rise in the total blood-cholesterol level was also observed, which suggested an increased lipid absorption. Of considerable interest was a diminution in the cough with decreased evidence of lung infection on roentgen-ray examination, a change that these writers attribute to better absorption of vitamin A brought about by increased motility of the bowel.

A low blood-sugar curve in the glucose-tolerance test is found in true celiac disease.² Andersen⁴⁰ has pointed out that the glucose-tolerance curve in pancreatic fibrosis, although usually flat, may show an initial sharp rise and a rapid fall, as in the hunger curves described by Harris. Normal values are encountered. The low rise of the curve in celiac disease was at first interpreted as a change secondary to diminished gastrointestinal motility. May, McCreary and Blackfan⁶ found, however, that when a solution of 3 per cent glucose containing as much glucose as was given ordinarily in a 10 per cent concentration was introduced intraduode-

nally in patients with celiac disease, the level of glucose in the blood did not rise more than 40 mg. per 100 cc. even if active intestinal motions were maintained by means of Mecholy. When patients recovered from celiac disease, however, a normal rise in the blood sugar occurred following the simple intraduodenal administration of glucose in a 3 per cent concentration. Although intestinal motility plays an important role in intestinal absorption, there must be in addition in celiac disease an impairment of absorption of glucose by the intestinal mucosa. No adequate explanation has been offered for the poor absorption of glucose when it does occur in patients with pancreatic fibrosis.

ROENTGENOLOGIC STUDIES

In both pancreatic fibrosis and celiac disease clumping of the barium meal in roentgenograms of the small bowel similar to that observed by Snell and Camp⁴⁶ in adults with steatorrhea and in vitamin B deficiency states⁴⁷ was found with regularity by Blackfan and Vogt,⁴⁸ and was explained by May and McCreary⁴⁹ by the impairment of peristalsis and tone and by segmentation of the bowel. Alternate segments showing spasm and dilatation with loss of the normal pattern of the valvulae conniventes characterize the roentgenologic picture. This abnormality in the motility of the bowel may be temporarily corrected by Mecholy.⁴⁴

Attwood and Sargent⁴⁹ have described the roentgen-ray appearance of the pulmonary lesions that are so consistently a part of the disease at any time after the first few weeks to months of age. They reported an increase in the density of hilar shadows, with loss of definition and prolongation outward into a surrounding mottling that gradually diminishes toward the periphery of the lung. The changes are bilateral and are symmetrically distributed about the roots of the lungs and the adjacent parenchyma. The changes in the upper lung fields are quite as marked as those at the bases. These writers warn against the danger of making an erroneous diagnosis of tuberculosis in patients in whom the illness is prolonged, because of the marked chronicity of the pulmonary lesions. Neuhauser⁵⁰ has divided the lung changes into two stages corresponding to the pathologic picture. The first is characterized mainly by emphysema and atelectasis dependent on the partial or complete obstruction of bronchi and bronchioles by the tenacious mucus or mucopurulent exudate. Atelectasis is at times difficult to recognize, since the small shadows of increased density resemble areas of pneumonic consolidation. Obstructive emphysema is identified with less difficulty by the decreased density, the bulging spaces and the

widening of the intercostal spaces. In the later or second stage, the roentgenologic changes become more marked, with patchy areas of peribronchial infiltration and areas of bronchiectasis. The process is marked toward the hilum, and the bronchovascular and interstitial markings radiating from each hilum are increased. The end stage is that of pneumonic infiltration, bronchiectasis and bronchiectatic abscesses, with varying degrees of atelectasis and obstructive emphysema. It should be stressed that these x-ray manifestations of pulmonary disease are by no means limited to patients with pancreatic achylia. They occur so frequently, however, in patients with this disorder that studies designed to confirm or exclude this diagnosis, such as analysis of pancreatic-enzyme activity, should be carried out whenever such changes are encountered.

TREATMENT

The outstanding disturbances produced in this disease, either by the pancreatic insufficiency or by the alterations elsewhere in the body, include absent or greatly reduced pancreatic-enzyme activity, particularly of trypsin and lipase; malabsorption of vitamin A; loss of nitrogen in stools; and upper respiratory obstruction and infection leading to bronchiectasis and bronchopneumonia. Treatment may be directed logically along these four channels. Pancreatic substitution therapy is indicated by the pathologic picture and the demonstration of pancreatic hypochylia or achylia. It has been found of value in infants and children and in adults with pancreatic insufficiency.^{27, 38, 40} The greatly diminished absorption of vitamin A that has been demonstrated by the vitamin A absorption test,^{43, 44} as well as by the occasional finding of histologic evidence of vitamin A deficiency,¹⁴ may be corrected either by enteral or parenteral administration of vitamin A.^{30, 40} Intramuscular injection of preparations of vitamin A in large doses has been recommended.³⁰ The marked loss of nitrogen in the stools may be corrected in part by pancreatic substitution therapy and in part by a direct replacement of lost nitrogen in the form of casein hydrolysate.³⁷ Infection in the lungs is an almost invariable accompaniment of the disturbance in nutrition. Since the most frequently found organism is *Staph. aureus*, and since it is one of apparently low virulence, chemotherapy is indicated, although difficulty is encountered in finding a completely effective form of specific therapy.

Flax, Barnes and Reichert³⁰ have recommended the parenteral administration of Prostigmine to improve the muscle tone in the intestinal tract and so permit enhancement of nutrition in general

and absorption of vitamin A in particular. They summarize their therapeutic regimen as follows: a high-calorie, high-protein, moderately low-fat and low-starch diet; pancreatin granules, 1.5 gm. daily; vitamin A, 50,000 international units daily, in divided doses; adequate amounts of vitamins B, C and D; and Prostigmine Bromide, 3.75 to 7.50 mg. three times daily. Andersen⁵¹ recommends a diet essentially similar to that used in celiac disease, with two important differences: hexose and sucrose, which can be utilized, are given instead of starch, and if pancreatin is administered a moderate amount of fat can be utilized. She used a diet high in protein, moderately low in fat and free from starch but not from sugar, and emphasizes the value of a caloric intake 30 to 50 per cent greater than that calculated for the given age to compensate for the loss of food in the stools. Although the parenteral injection of vitamin A concentrate or carotene was logical in theory, it was disappointing in practice. Much better results were obtained by the oral administration of large doses (15 drops) of percomorph or haliver oil three times a day.

At the Children's Hospital, Smith⁵² emphasizes the importance of good hygienic surroundings, with special reference to prevention of upper respiratory infection, and recommends the immediate and intensive treatment of all infections with some chemotherapeutic agent. In some infants a small maintenance dosage is continued for longer periods. The disturbed nitrogen metabolism is cared for most satisfactorily by the use of casein hydrolysate preparations, as described by Shohl and his co-workers.³⁷ Pancreatic substitution therapy is given in the form of minute granules each of which is enteric coated (Panteric Capsules, Parke Davis). The granules are sprinkled on the food and are given in amounts of 2 to 5 gm. daily in divided doses. Special attention is paid to a high vitamin intake with especially large doses of vitamin A. Glucose is added to the diet to increase the caloric content. Intravenous and parenteral fluids are given according to indications in the given case.

Until recently all patients with proved pancreatic fibrosis have died, as has been clearly shown in recent studies.⁵³⁻⁵⁸ Before pancreatic-enzyme studies were used, it was impossible to be certain of the diagnosis in patients said to have recovered from this disease. Recently a number of infants have been kept alive longer than was previously possible and some have improved markedly under a form of treatment similar to those discussed above.^{51, 52} The great power of regeneration possessed by the exocrine portion of the pancreas⁵⁹ gives hope for resumption of pancreatic function if the cause of the obstruction can be removed.

The form of treatment recognized for this removal, however, remains to be found.

In most cases the pulmonary lesions are responsible for death. Avoidance of infection is only one, albeit an extremely important, aspect of the problem. The markedly thickened mucus, responsible for the partial obstruction of the respiratory tract and the consequences thereof and for the pertussis-like cough, is one of the most important variable factors influencing the prognosis. It is representative of what may be present in other secretions in the body, if the disease is a systemic one, as pathological studies indicate.¹⁶

CONCLUSIONS

Adequate pancreatic substitution therapy, replacement of the large amounts of nitrogen lost in the stools and the administration of vitamin A and other therapeutic measures designed to correct the consequences of pancreatic achylia and the supposed error in fat absorption will do much to care for the pancreatic aspects of the problem. The disease is unfortunately much more than a lesion of the pancreas, and indeed, the great amount of attention paid to the pancreas in the recent literature, and even in this discussion, may serve to increase the neglect of the respiratory and other changes that emphasize the systemic nature of the process. Further studies are required to clarify and delimit the clinical disturbances associated with this disorder. Pathological studies²⁰ indicate that there exist combinations of organ involvement in this systemic disease the clinical counterparts of which have not yet been defined. The most frequently encountered combination is that of pancreatic and pulmonary disease, as emphasized above. In some cases the pancreas, lung and liver all show significant lesions, with biliary cirrhosis the most striking pathologic finding. Finally, involvement of the lungs and the liver, with no disease in the pancreas, and therefore absence from the clinical picture of those symptoms referable to pancreatic insufficiency, provides further evidence for the systemic nature of the underlying disease process, and places the lesion in the pancreas in its proper setting.

The studies that were undertaken to terminate the confusion of idiopathic celiac disease with pancreatic steatorrhea have satisfactorily accomplished their purpose. And they have done more. Several dissimilar clinical disorders—meconium ileus, chronic bronchopneumonia and pancreatic insufficiency and a celiac-like disease associated with chronic pulmonary disease—have all been found associated with the same obstructive pancreatic lesion, and valuable metabolic and thera-

peutic studies, suggested by the nature of this lesion, have been successfully accomplished. Finally, this apparently unrelated group of clinical disorders has been shown to possess logical interrelations by the demonstration that the pancreatic and pulmonary lesions are manifestations of a common disorder involving many secretion-forming structures in the body in a systemic disease. The definition of further clinical disturbances produced by this systemic disease and the clarification of the nature of the underlying process are tasks that remain to be accomplished. A satisfactory nomenclature, which has so far evaded the workers in this field, would do much, if not to hasten progress, at least to facilitate a discussion of this subject.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 29431

PRESENTATION OF CASE

A seven-and-a-half-week-old male infant was admitted to the hospital because of diarrhea.

The infant was delivered following eighteen hours of labor, but breathed and cried normally and weighed 8 pounds, 14 ounces. A formula containing Similac was used and the child seemed to tolerate it well. He continued, however, to pass meconium in small, frequent stools for the first six days, and he was given two doses of castor oil, following which he passed small yellow formed stools for one week. He left the maternity hospital on the tenth day, weighing 7 pounds, 14 ounces, on a formula consisting of 8 ounces of evaporated milk, 1 ounce of Karo and 16 ounces of water, with six feedings a day. He failed to gain weight and was admitted to a community hospital, where he remained for two and a half weeks. His stools at first were watery but later became formed and of normal color. He vomited considerably. The day following discharge, the stools became watery again, associated with vomiting but no fever. His physician tried Biolac without success. On evaporated milk and Karo, however, the stools became semi-soft, copious, excessively foul smelling and yellow, rapidly changing to gray. During the week before admission there were six to eight bowel movements a day. The baby's appetite was said to have always been good, but he was irritable. He had received 50 mg. of vitamin C daily, as well as capsules of vitamins A and D. There had been no hematemesis, melena, bloody stools or jaundice. No history of recent infection could be elicited.

A twenty-month-old sister had recently died of "pancreatic fibrosis" in the same local hospital. Another sister had died of peritonitis at one week of age in another local hospital.

Physical examination showed a thin, pale, undernourished, moderately dehydrated, underdeveloped, screaming infant, weighing 7 pounds, 4 ounces. The eyes, ears, nose and throat were normal. The lungs were clear. The heart was nor-

mal. The abdomen was moderately distended. There was moderately active peristalsis. The skin over the extremities and chest was loose. Examination was otherwise normal.

The temperature was 97°F.

The blood showed a red-cell count of 4,210,000, with 14.5 gm. of hemoglobin. The white-cell count was 17,400, with 37 per cent neutrophils, 53 per cent small lymphocytes, 9 per cent large lymphocytes and 1 per cent monocytes. The urine gave a + test for albumin, and the sediment contained 15 to 20 white cells and occasional red cells per high-power field. The stools were light gray, hard, formed, guaiac negative and positive for fat. A stool culture was negative for pathogenic bacteria. The blood protein was 4.2 gm. per 100 cc., the cholesterol 122 mg. per 100 cc., the chloride 101.7 milliequiv. per liter, and the sodium 130 milliequiv. per liter.

X-ray films of the chest were negative, and films of the skull showed a somewhat anteroposteriorly drawn-out skull, with relative overdevelopment of the posterior fossa. The sutures and fontanelles were open.

The baby was placed on a formula of evaporated milk 7 ounces, Karo 1 ounce and water 12 ounces. His appetite was good. During the first week the stools were yellow, soft to formed and only occasionally watery. They numbered two to four daily. There was a slight increase in weight. At the end of the first week, the formula was changed to evaporated milk 9 ounces, Karo 1 ounce and water 11 ounces, in six feedings. The stools became copious, gray and foul smelling, and the baby began to vomit. Duodenal-enzyme analysis showed absent trypsin. At that time a discharge summary received from the community hospital where he had been treated, stated that a diagnosis of idiopathic pancreatic fibrosis had been made and that he had been discharged on pancreatic extract, 2 capsules daily. The fasting carotenoid level was noted to have been 1.8 units per 100 cc., and the vitamin A level 7.5 units.

On the eighth hospital day, the baby was placed on pancreatic extract, 1 granule three times a day, 15 drops of Navitol, a teaspoonful of vitamin B complex and 25 mg. of cevitic acid. He did not pick up, and an attempt was made to mix Nutramigen and pancreatin with whole boiled milk, supplementing these by vitamin K and liver extract intramuscularly twice weekly. The red count was 2,970,000, with 11 gm. of hemoglobin, and the white-cell count was 10,000. The stools were formed, green to yellow, almost fat free but guaiac positive. The total blood protein was 3.9 gm. per 100 cc. The weight was 7 pounds. He refused about half his feedings or vomited most of those he took. At the end of the second week he

*On leave of absence.

was placed on a formula consisting of 18 ounces of 2 per cent milk and 1 ounce of Karo supplemented by 5 gr. of pancreatin, which was steadily increased until he was getting 5 gm. of pancreatin. Vitamin D was furnished by ultraviolet irradiation. He was given repeated small transfusions of whole blood, which raised the red-cell count to 5,900,000, with 17 gm. of hemoglobin, on the eighteenth hospital day. He had two transfusions of plasma. The baby's condition seemed to improve considerably. The weight was 7 pounds, 8 ounces, on the twenty-fifth day, at which time he was having four small bowel movements daily.

On the thirtieth hospital day the temperature rose to 101°F. and the white-cell count to 19,000 and the baby was noted to have a weak cough. Physical examination and x-ray films of the chest were negative. He was, however, placed on sulfadiazine. The following day he developed vomiting and diarrhea, was taken off fluids by mouth and placed on intravenous and subcutaneous fluids. On the thirty-second hospital day the temperature rose to 103°F. The eardrums appeared inflamed but paracentesis yielded no exudate. Lumbar puncture was negative. Blood cultures gave no growth. He developed increasing respiratory distress, but the x-ray films of the chest remained negative. The respirations dropped to 8, and the heart became weak. The veins were collapsed, and the blood dark. Whole-blood transfusion and intranasal oxygen brought no improvement, and the baby died on the thirty-fourth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. RALPH A. ROSS: The fact that this baby passed meconium stools for six days is significant, because ordinarily at the end of the third day meconium stools have ceased, and with an infant taking a reasonable formula, one expects to see beginning milk-curd stools. Apparently this was a matter of concern to the physicians in charge because the child was given two doses of castor oil.

The administration of castor oil in some circles has been used, I think, in an attempt to affect what is called meconium ileus, a rather rare instance of sticky meconium that cannot be passed on by the normal peristaltic movements of the bowel. In some hospitals the giving of castor oil has been made more or less routine on the third day, if there is any question about the stools. I believe, however, that castor oil is a drug that should never be used—perhaps I should say “hardly ever”—in the newborn period. If the expected effect of giving castor oil is to release the sticky meconium, it seems completely impossible that that can be accomplished by the administration of a violent irritant to the bowel. It is more likely that the meconium will completely obstruct

the bowel and that the hyperactivity of the gastrointestinal tract will lead to a disastrous outcome.

The loss of weight of 1 pound is more than should occur in a normal child at the age of ten days.

The foul-smelling gray stools point to the presence of excess amounts of fat.

One can only question whether the sister who died at the age of one week suffered from meconium ileus and had a rupture of the intestine with peritonitis.

On admission the infant's weight was 1 pound, 10 ounces, lower than at birth. He was only moderately dehydrated and was screaming, and was therefore not in collapse or shock from dehydration. A moderately distended abdomen in an emaciated child is an abnormal finding and points to some severe difficulty.

“The temperature was 97°F.” This low reading may have been due to exposure, but in an infant in such a debilitated state the low temperature may very well have been a sign of severe infection. The blood counts for a newborn infant were within normal limits. The white and red cells in the urine possibly point to some infection in the urinary tract.

The sodium was definitely low, which indicates loss of excessive amounts of sodium, probably through the gastrointestinal tract.

There is no indication that a gastrointestinal series was done. Is that correct?

DR. BENJAMIN CASTLEMAN: Yes.

DR. ROSS: “Duodenal-enzyme analysis showed absent trypsin.” That is a significant finding and almost pathognomonic. There is no note about presence of a lowered level of lipase in the duodenal enzyme. The level of amylase at this age is so low that it can barely be read.

The fasting carotenoid level was noted to have been 1.8 units and the vitamin A 7.5 units. These so-called “blue units” that are used to express the level of blood carotenoids and vitamin A are purely arbitrary. In this age group the normal range for carotenoids is between 7 and 10 units and for vitamin A around 15. Thus there was a marked reduction in these two fat-soluble vitamins or previtamins. The diagnosis of idiopathic pancreatic fibrosis would naturally lead to an attempt at substitution therapy, using one of the pancreatic extracts. Nutramigen is one of the casein hydrolysates, providing a mixture of protein break-down products, largely amino acids.

The stools became “almost fat free.” That may have been due to the fact that the diet was low in fat content. The lowering of the red-cell count, of the hemoglobin and of the total protein points to poor protein absorption. Vitamin D

was furnished by ultraviolet irradiation on the assumption that fat soluble vitamins would not be absorbed from the gastrointestinal tract.

The differential diagnosis in an infant of this age, with the long, complete story that we have, does not allow many possibilities. The obvious diarrhea, the inability to tolerate fat, the failure to gain and the enlarged abdomen, all point to some difficulty with intestinal absorption.

Celiac disease would be rather unusual at such an early age. It is a condition seen in infants and young children, usually appearing late in the first year of life, with the typical symptoms not often being seen until the beginning of the second year. The disease is not associated with any change in duodenal enzymes. There is another type of disease associated with intolerance of starch, in which fat may be properly absorbed but starch inadequately taken care of; in such cases the amylase content of the duodenal fluid is low. That again appears in an apparently normal child after six months of life and has a strong tendency to be familial. Syphilis has been reported to have produced fibrosis in the pancreas and the condition outlined here; however, although no specific statement is made, I should guess that this was not syphilis.

DR. CASTLEMAN: The blood Hinton test was negative.

DR. ROSS: Sprue, the vitamin B deficiency disease, certainly has never been proved at this early age. Mechanical obstruction to absorption in the gastrointestinal tract and short circuiting, as in gastrocolic fistula, are possibilities, but there is no evidence for them.

Congenital stenosis of the gastrointestinal tract, with impairment of absorption, as seen in tuberculous peritonitis with obstruction to the return of lymph from the intestinal tract, would not appear in an infant this young. The books say that heavy-metal poisoning may cause obstruction to absorption. There is no evidence in this child that such poisoning had occurred.

I am forced to the diagnosis that the other hospital made — namely, idiopathic fibrosis of the pancreas. In support of this diagnosis we have the family history of one other child with pancreatic fibrosis and the second one with a suspicion of the same disease. There were absent trypsin and increasing anemia and hypoproteinemia despite the administration of large amounts of blood; in other words the child was unable to manufacture its own protein. These signs are associated mainly with the disease that we know as idiopathic fibrosis of the pancreas. The low fat absorption, as evidenced by the rather

low cholesterol, carotenoids and vitamin A, certainly fits in with this picture. The variation in fluid metabolism that would result from large amounts of fluid in the loops of bowel that had been distended and were edematous may explain the low sodium. The one thing that is missing is the presence of respiratory infection. However, this child was so young that he possibly did not have time to develop the type of infection so classically seen in fibrosis of the pancreas after the first three or four months of life. Such infection can possibly be explained on the basis of inability to absorb fat-soluble vitamins, with the development of vitamin A deficiency, metaplasia of the epithelium of the respiratory tract and areas of infection. In this infant, however, there is no evidence that infection was the cause of death; quite possibly, even though physical examination and x-ray examination did not show it, Dr. Castleman may be able to point out evidence of pulmonary infection. The diagnosis of rickets, due to vitamin D deficiency, in a child this young and with so little growth is unlikely.

CLINICAL DIAGNOSES

Pancreatic fibrosis.
Otitis media.

DR. ROSS'S DIAGNOSES

Idiopathic pancreatic fibrosis.
Vitamin A deficiency.

ANATOMICAL DIAGNOSES

Idiopathic pancreatic fibrosis.
Pulmonary atelectasis, focal.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: This child did have idiopathic pancreatic fibrosis. At autopsy the child was quite emaciated but well developed. The only gross finding that was easily visible was focal atelectasis of the lung, but no real areas of consolidation. The pancreas appeared somewhat smaller than normal and was extremely firm. Microscopically there was marked interlobular and interacinar fibrosis throughout the pancreas, and many of the acini and ducts were dilated and filled with mucus (Fig. 1). Some showed definite cyst formation. I know very little about the pathology of this condition and have invited Dr. Farber to come down from the Children's Hospital to tell us more about it.

DR. SIDNEY FARBER: I was able to study the organs of the sibling mentioned in the record who died at the community hospital. The patient, who had much the picture that Dr. Castleman has just

described, was a girl twenty months of age with symptoms that began shortly after birth. The pancreas showed a more extreme degree of atrophy, dilatation of the acini and ducts and fibrosis than the one under discussion here. But the one here I regard as a fairly marked example of the disease. In addition, the sibling had a widespread bronchopneumonia caused by *Staphylococcus aureus*, and there was rather marked obstruction in the

structures, coalescence of the fibrous-tissue stroma and the formation of new fibrous tissue. The thick inspissated material is what one sees when one looks at the duodenal contents, which are thickened and sticky.

If the disease has run some months, the trachea and bronchi and the upper respiratory tract may be literally blocked by this very thick mucus, to which is usually added staphylococcal infection.



FIGURE 1. Photomicrograph of a Section of the Pancreas.

upper respiratory tract caused by inspissated mucus and purulent material.

I shall describe some of the changes we saw in this and other cases of pancreatic fibrosis. The pancreas may be normal in appearance or it may show the picture of marked atrophy. The normal portions of the pancreas stand out above the level of the diseased lobules, which are depressed, representing areas of atrophy and fibrous-tissue replacement. The clinical picture, however, may be produced by a pancreas that grossly appears normal. On microscopic examination the obstruction will be found in the small acini, and such obstruction causes pancreatic achylia in as great a degree as that produced by ligation of the main pancreatic ducts.

The term "cystic fibrosis" has been used, but there are no true cysts. Obstruction develops in the acini and is caused by inspissated pancreatic secretion, which is propelled with difficulty into the ducts. This, in turn, causes atrophy of the acinar

In this case, however, the main picture in the lung is not one of infection but rather one of obstruction. The major bronchi and the bronchioles are filled with inspissated material, and these infants may actually die of suffocation. The x-ray picture goes with these findings. Thus the same mechanism responsible for the pancreatic change appears to be responsible for the changes in the respiratory tract. Changes due to vitamin A deficiency are present in some but not all cases of this disease. Vitamin A deficiency, I believe, is not responsible for the occurrence of pulmonary infection.

The explanation for the obstruction, as well as the superimposed staphylococcal infection so often present, is found in the alteration of the character of the mucus produced by the glands of the trachea and bronchi. It is similar to the alteration found in pancreatic secretions in the pancreas. The material in the bronchial gland is thick and sticky and does not lubricate properly the mucosal surface of the trachea and bronchi. The organism

is not of great virulence as seen by the fact that little damage pathologically can be demonstrated even after the *Staph. aureus* is proved to have been present in the lung for one or two years. Similar changes may be found in the sublingual gland, duodenum, gall bladder, esophagus and bowel. One of the rare complications of the disease, which has occurred six times in our experience in recent years, is involvement of the liver in a form of cirrhosis that I have not encountered or seen described elsewhere. It is an essentially obstructive biliary cirrhosis. The bile capillaries are greatly distended and are filled with inspissated eosinophilic-staining material similar to the substance in the pancreatic acini and ducts. The obstruction causes atrophy of the liver drained by these bile capillaries and replacement fibrosis.

I have been forced to the conclusion that this disease is not a disease limited to the pancreas. The pancreas is merely one of many organs in the body affected by a general pathologic process involving secretory structures in many parts of the body. Wherever secretory structures are affected the fundamental change appears to be the same—the material secreted is more viscid, flows less readily than normal and, by mechanical action, causes obstruction to the duct system or gland system with an eventual fibrous-tissue replacement distal to the point of obstruction. There is sufficient evidence to say that vitamin A deficiency is a complication of the disease, not the cause of it. The exact cause is still unknown.

DR. CASTLEMAN: I might add that in our case there was no evidence of vitamin A deficiency. There was a small amount of mucus in the trachea and large bronchi and a very small amount in the bronchioles, which might have accounted for the focal atelectasis. There was no evidence of pneumonia. Examination of other mucous glands, such as the submaxillary gland and the duodenum, showed an early change, but nothing striking, probably because the child was so young.

CASE 29432

PRESENTATION OF CASE

A sixty-year-old woman entered the hospital because of persistent nausea and vomiting.

Eight days prior to admission the patient suffered with gaseous fullness and crampy lower abdominal pain. She passed large amounts of gas rectally, with some relief. Two days later she felt nauseated and vomited small amounts of bitter, yellow, nonbloody fluid. The nausea and intermittent vomiting continued to the day of admission, and she had been unable to retain anything except small amounts of broth. Bowel movements

had been regular and normal during the illness; the patient, however, took a laxative each day. The stools were not observed to be tarry, bloody or acholic. She had not been jaundiced, nor had she suffered with fever or chills.

The patient had been admitted to the hospital seventeen months previously, at which time the left breast was radically resected because of carcinoma. The axillary lymph nodes were reported to have been uninvolved. The family history was noncontributory.

Physical examination disclosed a well-developed and well-nourished woman. There was a well-healed scar over the left chest extending into the axilla. No nodules were felt in the scar line, right breast or axillas. The heart and lungs were normal. The abdomen was distended and quite tympanitic. No tenderness was elicited, and no masses were felt. Marked peristaltic rushes were audible over the entire abdomen. Questionable dullness was percussed on the left side of the abdomen.

The blood pressure was 132 systolic, 72 diastolic. The temperature, pulse and respirations were normal.

The white-cell count was 8500. The urine was normal, and the stool guaiac negative. A Hinton test was negative. A roentgenogram of the abdomen demonstrated several loops of slightly dilated small bowel in the left midabdomen. A barium enema passed to the junction of the descending colon and sigmoid, where it met a point of practically complete obstruction. During the fluoroscopic examination no barium was seen to pass beyond the obstruction. On the films, there was a small amount of barium proximal to the lesion. There were numerous diverticulums of the sigmoid, one of which was close to the point of obstruction. On one film there appeared to be a cavity in which there was a small amount of dilute barium. There was evidence of a small pressure defect in the sigmoid just distal to the lesion. Several loops of slightly dilated small bowel were observed, and there was a large amount of gas in the cecum. The right side of the pelvis showed evidence of Paget's disease.

On the day after admission a cecostomy was established, and ten days later the barium enema was repeated. This was again unsatisfactory, since the barium did not pass the point of obstruction.

An operation was performed on the seventeenth day after admission.

DIFFERENTIAL DIAGNOSIS

DR. CLIFFORD C. FRANSEEN: It is interesting to point out that this patient had bowel movements up to the time the barium enema was done, but it was not possible to pass barium beyond the

stricture. Of course that is a frequent occurrence, —that is, barium goes easily in one direction but not in the other in this type of lesion. The x-ray pictures will undoubtedly be of great assistance, and we should see them before proceeding.

DR. GEORGE W. HOLMES: This ought to be *the* case in which the findings are due to diverticulitis.

The film of the chest is negative. Those of the abdomen show the characteristic signs of obstruction, with accumulations of gas in the small bowel. So far as the x-ray is concerned there is no positive evidence of free fluid. The diverticula are quite large and are scattered throughout the lower sigmoid. Evidently the patient had some difficulty in retaining the enema. A retaining catheter was used, and apparently complete obstruction was demonstrated. I might add that the picture at the point of obstruction looks a little like tumor.

DR. FRANSEEN: Dr. Holmes says that this should be *the* case with diverticulitis, undoubtedly because we have recently discussed two cases with similar findings in which a diagnosis of diverticulitis was made only to have them both turn out to have been due to carcinoma. We shall have to review the findings to look for some evidence, other than the presence of diverticulums, for making the diagnosis of diverticulitis.

The first thing in sequence that seems to be of significance is the breast carcinoma that was operated on seventeen months previously. That is the only point in the history up to eight days before entry that gives any lead to a possible cause. The lymph nodes were uninvolved at the time of the breast operation; hence the likelihood of distant metastases is diminished, but certainly not excluded. On general principles, the first thing we ought to consider is a metastatic lesion. To my mind, a metastatic lesion that could produce this picture would be a little unusual because the obstruction to the large bowel was complete. A metastatic lesion is usually extrinsic, and would have to be extensive to produce complete obstruction by pressure on the large bowel. One could assume that there was some obstruction to the small bowel because of the dilated loops, and it is also conceivable that a metastatic lesion could have a loop of small bowel affixed to it, thus producing enough obstruction to the sigmoid to give this picture. It would be unusual, however, to have a single isolated metastasis like this from a carcinoma of the breast without other evidence of metastatic lesions.

Other things of extrinsic origin could have produced the picture—such as endometriosis. There is no way of proving any of these diagnoses,

however, and the case narrows itself down in large part, if one uses the statistical method of diagnosis, to a primary lesion in the bowel.

The two most likely diagnoses are carcinoma and diverticulitis, or both. Numerically, carcinoma is, of course, the most frequent. One thing that is against carcinoma is the lack of previous trouble. On the other hand, the short history is in favor of an inflammatory lesion in an area of diverticulosis. The absence of bleeding, although favoring diverticulitis, does not entirely exclude carcinoma. It is unusual, however, for a carcinoma to produce obstruction without previous symptoms or without bleeding. It is also unusual, at least in my experience, to have the obstruction of a carcinoma so complete without previous symptoms. There was really no lumen to the bowel at the point of tumor, since the barium enema showed complete obstruction. The evidence in favor of diverticulitis, on the other hand, is the presence of numerous diverticulums. Perhaps a carcinoma was present that mechanically obstructed a diverticulum and set up a diverticulitis. The presence of a small cavity is certainly evidence in favor of an inflammatory lesion—presumably an abscess draining into the bowel, since it was shown by barium enema. If one is going to bring the small bowel into the picture I cannot escape the impression that the x-ray findings there were entirely due to backing up of gas in the small bowel. The obstruction could also have been due to secondary ileus from an inflammatory lesion. Adhesion of a loop of small bowel to the sigmoid does occur, and it is more likely to occur in an inflammatory lesion than in carcinoma. In the late stages of carcinoma of the sigmoid, of course, it frequently happens. Another thing against an inflammatory lesion is that no tenderness was elicited on examination. One would expect some tenderness in a case of diverticulitis so severe that the bowel is obstructed; but this patient was sixty years old and we know that old people can have severe inflammatory lesions in the bowel with no tenderness or spasm to account for them. The temperature, pulse and respirations were also normal, which argues to some extent against an inflammatory process, but not entirely. The white-cell count was also normal.

I end up with an uncertain picture for either carcinoma or diverticulitis. It might, of course, be both, but on the basis of the evidence presented by the x-ray findings, by the history and by the other points that I have discussed, I believe that one should go on the basis of probabilities and put diverticulitis first, with strong reservation so far as carcinoma is concerned.

DR. FLETCHER H. COLBY: Does the fact that ten days after cecostomy complete obstruction was still present favor an inflammatory lesion?

DR. FRANSEEN: Not entirely. I am sure Dr. Smithwick will agree that after cecostomy is done for an obstructing carcinoma in the lower bowel the patient frequently has spontaneous bowel movements, the lumen opening up again. To my mind, your point argues in favor of diverticulitis.

DR. REGINALD H. SMITHWICK: In my personal experience it is rather unusual for diverticulitis to produce total and persistent complete obstruction. In the 65 patients on whom we have operated in this hospital in fifteen years, there are only 4 or 5 that really had complete obstruction by barium enema when they entered the hospital. In these the obstruction cleared up completely within two weeks after proximal decompression, so that my feeling is that if obstruction fails to let up it is more in favor of cancer than it is of diverticulitis.

DR. FRANSEEN: The one strong point in favor of carcinoma is the suggestion of protrusion of a mass into the lumen of the bowel.

DR. SMITHWICK: Another point is the location of the lesion in a case such as this. It is quite difficult to say by barium enema where the descending colon ends and where the sigmoid begins, but it is rare to have any surgical complication of diverticulitis above the upper end of the sigmoid. In this particular case it is probable that the point of obstruction was in the descending colon rather

than in the sigmoid. That also is in favor of cancer.

At the time of operation we were unable to tell whether this woman had diverticulitis or cancer, or both. She did have an inflammatory process and obvious diverticulums. The involved area was resected.

CLINICAL DIAGNOSIS

Carcinoma of sigmoid?
Diverticulitis with obstruction?

DR. FRANSEEN'S DIAGNOSIS

Diverticulitis of sigmoid?
Carcinoma of sigmoid?

ANATOMICAL DIAGNOSES

Adenocarcinoma of descending colon.
Diverticulosis coli.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The lesion in this case was a completely annular, constricting carcinoma, as well as multiple diverticulums. The diverticulums were distal to the cancer. I should say that the cancer was in the lower end of the descending colon rather than in the sigmoid.

DR. SMITHWICK: I cannot conceive how this patient could have gone up to a few days of the time of her hospital entry without any symptoms.

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MEDICAL ADVERTISING

In an editorial "Council Standards and Medical Advertising," which appeared in the October 9 issue of the *Journal of the American Medical Association*, it is stated that the business managers of various state medical journals are urging the breakdown of standards set by the Council on Pharmacy and Chemistry of the American Medical Association. Since the *Journal* is one of the periodicals mentioned by name, refutation of the accusation seems justifiable.

For many years the *Journal* has obtained the majority of its contracts covering nationally advertised products from the Cooperative Medical

Advertising Bureau, which was created in 1913 by the Board of Trustees of the American Medical Association. All accounts are handled through the office of the Bureau in Chicago, and this service is paid for on a commission basis. Since the Bureau is a nonprofit organization, a generous refund is made to the *Journal* at the end of each fiscal year. As part of the agreement, the *Journal* agrees to limit advertising to pharmaceutical products that have been accepted by the Council on Pharmacy and Chemistry of the American Medical Association, and failure to abide by this clause has provoked the serious accusation referred to above.

The *Journal*, at the moment, has advertising contracts with two local firms that manufacture nonaccepted products. In each instance, the drugs had never been submitted to the Council for approval, and careful investigation revealed that they were being used and recommended by authoritative physicians; furthermore, no unwarranted claims have been made in the advertising copy. All this has been done with the full knowledge of the Cooperative Medical Advertising Bureau, which, incidentally, has failed to reply to a letter dated August 11, 1943, in which it was stated that the *Journal* intended to continue with the advertising of this type unless specifically told not to do so by the Advisory Committee of the Bureau.

Another difficulty often leading inadvertently to the advertising of nonapproved drugs arises from the fact that Bureau-sponsored firms often submit copy covering such products directly to the medical journal. Unless the business manager is alert, such copy is likely to be accepted routinely.

By and large, there appears to be no concerted effort to break down, or even weaken, the standards of the Council on Pharmacy and Chemistry. Certainly there is little excuse for the statement, "The time should long since have passed when leaders of medical organizations consent to permit the exploiters of unestablished proprietary remedies to pay the bulk of printing and publishing bills of the medical journals that are supposed to

represent scientific medicine," or for the exhortation, "Let us keep the good name unsullied; its value is far above that of jewels or gold." The editorial and business staffs of the majority of state medical journals fully appreciate the good that has been accomplished by the efforts of the Council on Pharmacy and Chemistry and have no intention of "upsetting the apple cart." On the other hand, it should be appreciated that federal regulations regarding new drugs and labeling are much stricter and much more rigidly enforced than they were thirty-five years ago; that approval by the Council of effective and valuable drugs that are widely used is often unduly delayed or withheld because of minor infringement; and that the chief revenue of the majority of state medical journals is that derived from medical advertising. Previously, only one of the three members of the Advisory Committee of the Co-operative Medical Advertising Bureau had been connected with a state medical journal. Quite recently, however, the Board of Trustees of the American Medical Association, owing to pressure brought to bear by representatives of the state journals, has appointed two additional members, both of whom are editors. It is hoped that some arrangement regarding medical advertising that is advantageous both to "scientific medicine" and to the state journals will be forthcoming.

MISSILE WOUNDS OF THE SKULL AND ITS CONTENTS

It is earnestly recommended that all physicians take the trouble to read the leading article in the August 21 issue of the *Lancet*. Entitled "Treatment of Head Wounds Due to Missiles," it is an analysis of 500 cases treated during nearly two years by a mobile neurosurgical unit of the Royal Army Medical Corps in the Middle East. The author, Major P. B. Ascroft, visited Boston last May, at which time he gave a memorable talk on the same subject before a joint open meeting of the Boston Surgical Society and the Boston Society for Neurology and Psychiatry. Those fortunate

enough to have been present can scarcely forget the modesty with which he cited the extraordinary results he and his team had attained. The paper contains all that he said at that time, as well as certain other data. It is obvious that any organization that can deal with over four hundred missile wounds of the skull and its contents with a mortality of only 10.6 per cent and in addition return 71 per cent of the survivors to duty in an army geared to total war speaks with authority about its specialty.

The author and head of the unit was a trained neurosurgeon whose reputation had already been established in England before undertaking this particular assignment. Assisting him were a neurologist, Major Kremer, an anesthetist, Major Cope, and two assistant surgeons, Major Hooper and Captain Northcroft. All their reported methods and conclusions have civilian as well as military application, but certain of their points bear repetition, particularly those regarding compound fractures of the skull not sustained in battle. By categorically stating that it is better not to operate in forward areas provided the patient can reach a fully equipped base hospital within forty-eight to seventy-two hours of injury, by emphasizing the importance of a mechanical sucker and by failing to mention irrigation as a therapeutic agent in dealing with these wounds, as well as in other details of resuscitation, anesthesia, lumbar puncture and so forth, they confirm under battle conditions the opinion of a group of American neurosurgeons about the value of certain procedures relative to the time and method of dealing with civilian compound fractures of the skull, and settle a debate that has exercised this specialty for some years.

It is interesting to note also that Major Ascroft recommends the use of a plaster-of-Paris bandage as a means of securing the first dressing applied at the front, as well as to protect the patient's head. This is in line with the Russian experience as detailed by Vladimir Lebedenko, surgeon and professor at the First Moscow Medical Institute, at the meeting of the American Neurological Society

in New York last May. So far as is known, this work, equally as authoritative as that reported in the English paper, has not as yet been published. Lebedenko, however, considered this therapy of sufficient importance to bring samples of such plaster casques with him from Russia. In addition, Major Ascroft's suggestion that the plaster be also used to carry a sketch of the wound should not be lost sight of. Lebedenko's reported conclusions relative to transportation, preferable locale for operative interference and proper time of operation after injury correspond closely to those reached by Major Ascroft.

It is axiomatic that the English report should be made required reading by every member of the medical departments of the Army and Navy, even should it prove necessary to reproduce it in its entirety by photostating, mimeographing or any other suitable method. In particular, copies should be made available at once to the front-line hospitals and personnel, because the conclusions differ so fundamentally from those previously authorized for publication by the War Department, which were largely reached shortly after World War I and which have been influenced little, if at all, by advances made in traumatic civilian neurosurgery in the intervening years.

All civilian surgeons should read this paper as well. Familiarity with its contents will, among other things, do much to destroy outworn shibboleths and help the overworked local doctor speak with conviction when he advocates moving the civilian prototypes of such patients to the large medical centers. Responsibilities he neither wants nor is equipped to carry on his own shoulders will be thus shifted to surgeons with better facilities and more appropriate training—with consequent benefit to the patient, the community, the doctor and the war effort.

MEDICAL EPONYM

HINES-BROWN TEST

This test is described by Drs. Edgar A. Hines, Jr. (b. 1906) and George E. Brown (1885-1935)

in an account entitled "A Standard Stimulus for Measuring Vasomotor Reactions: Its application in the study of hypertension," which appeared in the *Proceedings of the Staff Meetings of the Mayo Clinic* (7: 332-335, 1932). A portion of the article follows:

The subject is placed at rest for twenty minutes and the blood pressure is taken every five minutes until a constant level is obtained. Then one hand is immersed above the wrist in ice water for twenty to thirty seconds. The temperature of the water varies from 4° to 5°C. The systolic and diastolic blood pressures immediately rise, and then return to the basal level in from one to two minutes. . . .

It was found that among subjects . . . with organic forms of hypertension, the average increase of systolic and diastolic pressures was greatest for all the subjects studied. . . .

A later report on the results of this test in 571 normal and hypertensive subjects appears in the *American Heart Journal* (11: 1-9, 1936).

R. W. B.

OBITUARY

HALBERT GREENLEAF STETSON

1868-1943

On September 15, 1943, Dr. Halbert G. Stetson, of Greenfield, president of the Massachusetts Medical Society in 1931 and 1932, died at his home after more than a year of failing health, occasioned by a decompensated heart. Born in Greenfield on May 8, 1868, he was educated in the public schools of Orange and at New Salem Academy, acquiring his medical education at the College of Physicians and Surgeons of Baltimore, from which he graduated in 1895. He immediately began practice in Greenfield, which he continued to within a few months of his death, although he had done little surgery for several years.

In 1899 he formed a partnership with Drs. George P. Twitchell and Charles F. Canedy, which continued until the death of Dr. Twitchell in 1930, Dr. Canedy having died in 1925.

In 1897 he married Frances A. Gildart, of Salisbury, New Brunswick, who died in 1920. They had one son, Maurice H., now living in Kalamazoo, Michigan. In 1923 he married Anna B. MacKenzie, then head nurse at the Franklin County Hospital, who survives him.

His medical affiliations included membership in the American Medical Association, Massachusetts Medical Society, American College of Surgeons, Connecticut River Valley Medical Association, and New England and New York Association of Railway Surgeons.

Although surgeon for the Boston and Maine Railroad since 1903 and medical examiner of Franklin County since 1921, his chief interest was in the Franklin County Hospital, of which he was chairman of the Board of Trustees. He had much to do with the building and development of the present hospital, which was completed in 1910, and in 1938 donated a library in honor of his former partners, Drs. Twitchell and Canedy. This was named "The Stetson Library," by the hospital staff and a bronze plaque was placed on the wall in his honor. In addition he had served in several civic capacities, including president of the Greenfield Chamber of Commerce and chairman of the School Committee.

His chief hobbies, aside from the hospital, comprised books and postcards and attendance at medical meetings.

Dr. Stetson was a man of strong character and had the respect of all who knew him.

A. H. E.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR SEPTEMBER, 1943

RÉSUMÉ

DISEASES	SEPTEMBER 1943	SEPTEMBER 1942	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	122	9	14
Chicken pox	114	105	84
Diphtheria	15	9	9
Dog bite	901	846	918
Dysentery, bacillary	23	6	17
German measles	59	68	22
Gonorrhea	430	521	510
Measles	189	150	138
Meningitis, meningococcal	51	6	4
Meningitis, other forms	7	3	•
Meningitis, undetermined	3	0	•
Mumps	150	248	144
Pneumonia, lobar	114	192	120
Salmonella infections	30	33	5
Scarlet fever	397	315	168
Syphilis	482	460	427
Tuberculosis, pulmonary	217	252	239
Tuberculosis, other forms	27	12	23
Typhoid fever	2	3	9
Undulant fever	2	4	4
Whooping cough	301	778	546

*Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

COMMENT

The increase in poliomyelitis cases commented on in the August report has been considerably accelerated during September. The number of cases for this month was approximately nine times the seven-year median. This figure, nevertheless, is not high if judged by previous standards, and this year's outbreak on the whole will probably rank as a relatively minor one.

Meningococcal meningitis is still at a high level, nearly thirteen times the seven-year median, and there was a moderate rise over last month's figure. This may indicate

that the high prevalence may continue into the next season.

Diphtheria shows a slight increase this month, owing to 8 cases in a small town that has done little immunizing for the past few years.

Scarlet fever did not drop to the usual low seasonal level. This is the twenty-fourth consecutive month in which the number of cases exceeded the number reported the same month the previous year.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Attleboro, 2; Bedford, 1; Belmont, 3; Berkley, 1; Beverly, 23; Boston, 7; Braintree, 3; Brockton, 2; Cambridge, 1; Fall River, 6; Framingham, 1; Hinsdale, 2; Holliston, 1; Holyoke, 1; Hopkinton, 1; Lee, 2; Lynn, 11; Malden, 1; Mansfield, 1; Marblehead, 1; Maynard, 1; Medford, 1; Melrose, 1; Milton, 1; Natick, 1; Newton, 1; North Attleboro, 1; North Brookfield, 1; Norton, 1; Norwood, 2; Peabody, 2; Pittsfield, 3; Quincy, 2; Reading, 1; Revere, 1; Salem, 8; South Hadley, 1; Somerville, 1; Southbridge, 3; Springfield, 1; Swampscott, 1; Truro, 1; Wakefield, 2; Waltham, 4; Watertown, 3; Wenham, 2; Weston, 1; Weymouth, 1; Wilbraham, 1; Worcester, 1; total, 122.

Diphtheria was reported from: Arlington, 1; Blackstone, 1; Boston, 1; Boxboro, 8; Easthampton, 1; Taunton, 1; Weymouth, 1; Woburn, 1; total, 15.

Dysentery, bacillary, was reported from: Becket, 2; Boston, 2; Lawrence, 1; Malden, 1; Holyoke, 4; Melrose, 2; Northampton, 4; Wellesley, 1; Wilbraham, 1; Woburn, 5; total, 23.

Encephalitis, infectious, was reported from: Amherst, 1; Lynn, 1; Malden, 1; Stoughton, 1; total, 4.

Malaria was reported from: Amherst, 1; Camp Edwards, 1; Chelsea, 1; Fort Banks, 8; Leominster, 1; Revere, 1; Springfield, 1; total, 14.

Meningitis, meningococcal, was reported from: Acushnet, 1; Barnstable, 3; Boston, 14; Brookline, 1; Camp Edwards, 1; Chelsea Naval Hospital, 2; Dudley, 1; Fall River, 2; Fort Devens, 3; Hanover, 1; Holyoke, 1; Lowell, 3; Lynn, 1; Malden, 1; Northbridge, 1; Norfolk, 1; Revere, 1; Somerset, 1; Somerville, 2; Southbridge, 1; Wareham, 1; Westfield, 1; Weymouth, 1; Winthrop, 1; Worcester, 5; total, 51.

Meningitis, other forms, was reported from: Fall River, 1; Lawrence, 1; Lynn, 1; New Bedford, 1; Springfield, 1; Wilbraham, 1; Worcester, 1; total, 7.

Meningitis, undetermined, was reported from: Gloucester, 1; Medford, 1; Worcester, 1; total, 3.

Salmonella infections were reported from: Becket, 1; Beverly, 1; Brockton, 1; Cambridge, 2; Haverhill, 8; Lexington, 1; Lowell, 1; Pittsfield, 1; Somerville, 1; Templeton, 11; Wakefield, 1; Waltham, 1; total, 30.

Septic sore throat was reported from: Boston, 1; Marion, 4; Milton, 1; West Springfield, 1; total, 7.

Tetanus was reported from: Billerica, 1; Boston, 1; Haverhill, 1; Lowell, 1; Peabody, 1; total, 5.

Trachoma was reported from Hudson, 1; total, 1.

Trichinosis was reported from: Boston, 1; Westwood, 1; total, 2.

Typhoid fever was reported from: Gardner, 1; Malden, 1; total, 2.

Undulant fever was reported from: Adams, 1; North Brookfield, 1; total, 2.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Salem	November 1	Paul W Hugenberger
Haverhill	November 3	William T Green
Lowell	November 5	Albert H Brewster
Pittsfield	November 15	Frank A Slowick
Springfield	November 17	Garry deN Hough, Jr
Brockton	November 18*	George W Van Gorder
Worcester	November 19	John T O'Meara
Fall River	November 22	Eugene A McCarthy
Hyannis	November 23	Paul L Norton

*Date changed because of holiday

WAR ACTIVITIES

CIVILIAN DEFENSE

The following notice was recently released by Dr George Bachr, chief medical officer of the Office of Civilian Defense, Washington, D C

Rumors that civilian defense is no longer necessary have recently been spread by irresponsible persons. These rumors are thoughtless or calculatingly subversive, for they are not supported by Army authorities responsible for our coastal defenses or by the present military situation.

Fortunately, the success of our armed forces overseas has saved us thus far from experiencing the horrors of enemy bombing to which the cities of our allies are being subjected. In the opinion of the best military authorities our coastal areas and industrial centers will not be free of the danger of enemy attack from the air or of widespread sabotage until the last day of the war.

Civilian defense is needed also as one of the essential measures for safeguarding internal security. This is especially true of the Emergency Medical Service. If we had not created a nationwide organization for civilian defense two years ago, we would be obliged to organize one today for home security. Disasters of all kinds have increased because of the tremendous speeding up of our great industries, the overburdening of our railroads and the inexperience of hundreds of thousands of new war workers. Our police and fire departments, our public works and utility services and our hospitals, on which we depend for protection, are being increasingly depleted of trained personnel. We must therefore strengthen our voluntary protective services throughout the land. Along the Pacific and the Atlantic coasts these services must be especially strong in volunteer personnel and equipment to guard us against the hazards of enemy attack and sabotage until that day when the Army advises us that the danger is ended.

MISCELLANY

FIFTIETH ANNIVERSARY OF TUFTS COLLEGE MEDICAL SCHOOL

The grand assembly of the Fiftieth Anniversary of Tufts College Medical School was held on October 6 in Boston and was attended by 940 medical alumni and students. Among the speakers were Harold E. Sweet

president of the Board of Trustees of Tufts College, Dr Alonzo K Paine, professor of obstetrics, Dr Karl T Compton, president of the Massachusetts Institute of Technology, Captain A Warren Stearns (MC), USNR, dean-on leave, Dr Louis E Phaneuf, professor of gynecology, Commander Bartholomew W Hogan (MC), USN, and Dr Leonard Carmichael, president of Tufts College.

President Carmichael read a letter that he had received from President Roosevelt, in which the accomplishments of the medical school during the fifty years subsequent to its founding were praised and well wishes for the coming years were given. He announced that \$746,000 has been raised toward the \$850,000 Building Fund goal. He also acknowledged a contribution of \$125,000 by Edward Cohen toward the Building Fund. The total was exclusive of contributions that were made for various other specific purposes in connection with the medical school.

The Fiftieth Anniversary Committee consisted of Dr Phaneuf, chairman, Dr Carmichael, Capt Stearns, Dr Dwight O'Hara acting dean, and Dr Harry Blotner, secretary treasurer of the Tufts Medical Alumni Association.

RENEWAL OF AWARD TO SHARP AND DOHME

Sharp and Dohme, originators of the process by which dried blood plasma is made, and sole manufacturers of the first nine months' supply of this vital material for the armed services, was awarded the Production Army-Navy Award for the second time on Saturday, October 16. In a letter to the workers at the Philadelphia plant and the Glenolden laboratories of Sharp and Dohme, Robert P Patterson, Under-Secretary of War, stated: "You have continued to maintain the high standards that you set for yourselves six months ago. The White Star, which the renewal adds to your Army-Navy Production Award flag, is the symbol of appreciation from our armed forces for your continued and determined effort and patriotism." Sharp and Dohme's pioneer work in developing the methods and equipment necessary for the production of dried plasma is one of the most important contributions of the biological industry and has already resulted in great saving of life through transfusion of plasma at the scene of battle.

NOTES

Dr Joe V Meigs has recently been appointed surgeon in charge of gynecology at the Palmer Memorial Unit of the New England Deaconess Hospital. The Gynecologic Tumor Clinic of the Out Patient Department, which for many years had been under the direction of the late Dr G A Ireland Jr, will be under the guidance of Dr Meigs.

Dr Charles F McKhann has recently accepted the position as assistant to the president of Parke, Davis and Company and will devote his entire time to the scientific activities of the company. From 1936 to 1940, Dr McKhann was associate professor of pediatrics and communicable diseases at the Harvard Medical School and a member of the staff of the Children's Hospital, he then

joined the faculty of the University of Michigan, serving as professor of pediatrics and communicable diseases at the Medical School and as professor of maternal and child health at the School of Public Health.

CORRESPONDENCE

PLUMMER-VINSON SYNDROME

To the Editor: In your leader on the Plummer-Vinson Syndrome in your issue for July 22 you suggest that Kelly's name should be added to that of Paterson in discussing the upper-dysphagia-with-anemia syndrome. My reason for not mentioning Kelly is the same as my reason for no longer mentioning Plummer and Vinson. Paterson's first description of the condition was published in the *British Medical Journal* in 1906 (2:355) — thirteen years before his fuller description mentioned by you and before Kelly's. The priority is therefore quite clearly Paterson's and not Kelly's.

ARTHUR HURST

Red Gables
Headington, Oxford, England

DEPRIVATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held on October 6, the Board voted to revoke the license to practice medicine in Massachusetts of Dr. Manford R. Spalding, 129 Central Street, Auburn.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

BOOK REVIEWS

Athletic Injuries: Prevention, diagnosis and treatment. By Augustus Thorndike, M.D. Second edition. 8°, cloth, 216 pp., with 105 illustrations. Philadelphia: Lea and Febiger, 1942. \$3.00.

The second edition of this book has been thoroughly revised in the light of recent advances in the physiology of physical fitness, and the chapter on physical therapy has been rewritten with the assistance of Dr. Arthur L. Watkins. The manual should be popular with all those having to do with sports and physical culture. It is well printed, with a good type, and is of handy size.

The Clinical Application of the Rorschach Test. By Ruth Bochner, M.A., and Florence Halpern, M.A. With an introduction by Karl M. Bowman, M.D. 8°, cloth, 216 pp., with 3 graphs. New York: Grune and Stratton, 1942. \$3.00.

This comparatively new test is now widely used by psychiatrists. The test itself is simple in that the subject reports his interpretation of ten standardized ink blocks, pointing out everything that is revealed in or suggested by the outline of the figures. The results are then interpreted, a fairly complicated procedure only to be comprehended after considerable study under expert guidance. The aim of the test is to study the personality traits in the individual. This can, naturally, be done by prolonged personal investigation, but the time will be greatly shortened if the Rorschach test proves to be valuable. At pres-

ent the test should be left in the hands of those most competent to carry it out, since it is not something that can be widely applied by unskilled workers. This book will help anyone to understand the test as it is done by the authors, both of them qualified psychologists formerly associated with the Bellevue Psychiatric Hospital.

The test itself cannot be regarded as infallible and there are still many controversial points about its value. It has, however, established itself, probably permanently, in the psychiatric clinics as an important test for personality. This book, giving the known facts regarding the test and its interpretation, is an important addition to the current literature. A number of typographical errors need correction.

Synopsis of Materia Medica, Toxicology and Pharmacology. By Forrest R. Davison, M.Sc., Ph.D., M.B. Second edition. 12°, cloth, 695 pp., with 45 illustrations. St. Louis: The C. V. Mosby Company, 1942. \$5.75.

The first edition of this work was published in 1940, and it has now been found necessary to publish a second edition, which has been revised to include information on a large number of new drugs. The general plan of the work has not been changed, but in nearly every section important additions and deletions have been made. The revision conforms to the latest edition of the *National Formulary*, the twelfth edition of the *Pharmacopoeia of the United States* and the *British Pharmacopoeia*. The chapter on sulfonamide drugs has, of necessity, been enlarged.

An attempt has been made to keep the volume moderate in size, and this has led, unfortunately, to the use of a rather small type. The book also has been printed on coated stock, which makes it rather heavy for its size; a lighter paper would have made the volume easier to handle.

Memorable Days in Medicine: A calendar of biology and medicine. By Paul F. Clark, Ph.D., and Alice S. Clark. 12°, cloth, 305 pp., with 29 illustrations. Madison, Wisconsin: The University of Wisconsin Press, 1942. \$2.00.

This calendar of birth and death dates of noted men in the field of biology and medicine is a useful compilation, especially for those who have to plan regular exhibits for public display. The selection is purely a personal one of the authors and therefore will not meet the ideas of all those interested in the history of medicine. It seems incongruous to include the birthdays of the Virgin Mary and Leif Ericson.

One inaccurate entry is of considerable local interest. Under date of November 27, 1782, it is stated that the Harvard Medical School was established by the Corporation of Harvard College and that three professorships were then voted to John Warren, Benjamin Waterhouse and Aaron Dexter. The records of the Corporation show that on September 19, 1782, a report embodying a plan for the formation of a medical school was adopted, and that on November 22 one professor was appointed, namely, John Warren, who managed all branches of the new school. Benjamin Waterhouse was elected on December 24, 1782, and Aaron Dexter was not voted in until May 22, 1783. It was not until October 7, 1783, that Warren and Waterhouse were inducted into office with much ceremony.

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STUDIES ON THE DESTRUCTION OF RED BLOOD CELLS*

III. Mechanism and Complications of Hemoglobinuria in Patients with Thermal Burns: Spherocytosis and Increased Osmotic Fragility of Red Blood Cells

SHU CHU SHEN, M.D.,† THOMAS HALE HAM, M.D.‡
WITH THE ASSISTANCE OF ELEANOR M. FLEMING, A.B.§

BOSTON

HEMOGLOBINURIA, the excretion of extra cellular hemoglobin in the urine, is recognized as an early complication of severe thermal burns. It is a sign of rapid destruction of red blood cells producing, in the plasma, free hemoglobin, which is usually excreted promptly by the kidney.¹⁻³ In this paper observations are reported on the changes in the blood and in the urine and on the kidney complications occurring in 14 patients with moderate or severe thermal burns 10 of whom showed hemoglobinuria. Experimental studies on the effect of heating human red cells and on the effect of injection into the dog of heated canine red cells will be outlined briefly and reported in more complete form elsewhere.

In the literature on thermal burns, hemoglobinuria has infrequently been reported as a complication of severe third degree burns involving usually half or more of the body surface.⁴⁻⁶ Cope and Rhinelander⁷ reported 9 cases of hemoglobinuria in patients burned in the Coconut Grove disaster. Hemoglobinuria, according to Wilms⁶ was not a constant finding in severe burns. It lasted for only one or two days and the amount of blood destroyed was not sufficient to endanger the patient's life. Oliguria and albuminuria however, were the usual consequences of severe second degree or third degree burns, whether or not hemoglobinuria was present. Albuminuria lasted five days or longer. Marchand⁸ in a critical re-

view of the pathology of thermal burns found that the renal lesion of so called "burn nephritis" is similar to that produced by hemoglobinuria due to other causes. Experimentally, hemoglobinuria has been demonstrated in animals burned by scalding.^{9,10} The heating of blood to 52 to 65°C in vitro^{9,15} and the apparent heating of blood in vivo in burned animals^{10,16,19} have both produced progressive fragmentation of the red cells, with the formation of spherocytes and microspherocytes. Pfeiffer¹⁹ found that destruction of erythrocytes by heat was evidenced by the immediate occurrence of hemoglobin in the plasma of anesthetized animals burned by scalding, with a rise in subcutaneous temperature as high as 63°C. Von Lesser¹⁰ observed hemoglobinemia and hemoglobinuria in burned animals, in normal animals transfused with blood from a burned animal, and in normal animals injected with homologous blood heated to 60 or 62°C in vitro. The red cells with abnormal morphology were rapidly removed from the animal's circulation and presumably destroyed. Spiegler¹² and Isaac Brock and Minor¹ confirmed the morphologic changes occurring in heated blood and observed that red cells heated to above 50°C were increased in osmotic fragility. No hemolysins or agglutinins were found in the plasma or serum of burned animals by Burlingham¹³. Spiegler noted the lack of toxic manifestations when heated blood was injected into dog.

METHODS OF INVESTIGATION

Following the Coconut Grove disaster samples of urine showing hemoglobinuria were obtained for analysis. It was impossible in many cases to secure complete urine specimens during the first forty-eight hours because of incontinence and because of the complex nurs-

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Laboratory in Thonike Memorial Laboratory.

TABLE 1. *Observations on 14 Patients with Moderate or Severe Thermal Burns, of Whom 10 Showed Hemoglobinuria.*

CASE No.	HOSPITAL No.	SOURCE OF BURN	AGE	SEX	PERIOD OF SURVIVAL AFTER BURN	AREA OF BODY BURNED			INTERVAL AFTER BURN
						TOTAL BURN	SECOND DEGREE	THIRD DEGREE	
			yr.			%	%	%	
1	1088982	Cocoanut Grove	45	M	25 hr.	65			26 hr.
2	1088948	Cocoanut Grove	33	F	29 hr.	65			26 hr.
3	1088889	Cocoanut Grove	50	M	42 hr.	45			37 hr.
4	1088926	Cocoanut Grove	29	F	79 hr.	50			22 hr. 36 hr. 60 hr.
5	1088885	Cocoanut Grove	25	M	5½ d.	45	15	30	44 hr. 63 hr. 88 hr.
6	1088965	Cocoanut Grove	35	F	8½ d.	45	30	35	36 hr. 3 d 4 d 5 d 6 d 7 d
7	1088943	Cocoanut Grove	29	F	13 d.	45	15	30	18 hr. 36 hr. 3 d 4 d 5 d 6 d 7 d 9 d 10 d 11 d 12 d
8	1088892	Cocoanut Grove	22	M	Living	55	10	45	36 hr. 4 d 5 d 7 d 9 d 10 d 16 d. 21 d
9	1094717	In bed	50 (?)	F	5 hr.	30	5	25	2 hr.
10	1091461	Explosion of oil stove	40	F	5 d.	20			30 hr. 46 hr. 66 hr.
11	113422	In bed	32	M	9 d.		3	17	2 hr. 11 hr. 32 hr. 3 d 6 d
12	1091512	In bed	32	F	28 d.	65	20	45	3 hr. 10 hr. 25 hr. 34 hr. 50 hr. 74 hr.
13	1094057	In bed	50	M	32 d.	55	10	45	38 hr.
14	1103634	In dwelling	37	F	Living	15	3	12	½ hr. 2 hr. 3 hr. 4½ hr. 5 hr. 13 hr. 17 hr. 37 hr. 3 d 5 d 9 d 12 d 17 d

TABLE 1 (continued)

Case No	DEGREE OF INCREASE ABOVE NORMAL	OSMOTIC FRAGILITY OF RED CELLS								SPHEROCTES	
		DEGREE OF HEMOLYSIS								INTERVAL AFTER BURN	PER CENT
		1%	2.5%	5%	10%	20%	30%	40%	95%		
		% NaCl	% NaCl	% NaCl	% NaCl	% NaCl	% NaCl	% NaCl	% NaCl		
1	+	0.63	0.56	0.54	0.51	0.45	0.43	0.40			
2	++	0.67	0.59	0.55	0.4	0.39	0.35	0.29			
3	±	0.56	0.47	0.43	0.41	0.40	0.33	0.29		36 hr	3.0
4	++	0.67	0.63	0.58	0.52	0.42	0.41	0.40			
	+	0.59	0.53	0.49	0.45	0.40	0.38	0.34		36 hr	11.0
	+	0.59	0.53	0.47	0.43	0.38	0.35	0.29		60 hr	9.0
5	+	0.59	0.56	0.52	0.48	0.40	0.36	0.25		2 d	1.0
	0	0.47	0.45	0.44	0.43	0.40	0.37	0.26		3 d	0.8
	0	0.49	0.47	0.45	0.43	0.39	0.36	0.25			
6	0	0.45	0.43	0.42	0.41	0.37	0.35	0.29		2 d	0.2
	0	0.45	0.43	0.42	0.41	0.37	0.34	0.27			
	0	0.47	0.44	0.43	0.41	0.37	0.35	0.31		6 d	1.2
	0	0.48	0.47	0.45	0.44	0.38	0.34	0.29			
	0	0.45	0.43	0.42	0.40	0.34	0.29	0.25			
	0	0.47	0.45	0.43	0.42	0.34	0.31	0.25			
7	±	0.55	0.50	0.46	0.44	0.39	0.35	0.23		4 d	1.3
	0	0.48	0.44	0.43	0.42	0.38	0.35	0.29		5 d	0.8
	0	0.44	0.41	0.40	0.39	0.35	0.33	0.29		6 d	0.6
	0	0.46	0.44	0.43	0.42	0.37	0.34	0.29		8 d	0.8
	0	0.49	0.48	0.45	0.43	0.40	0.37	0.29			
	0	0.49	0.47	0.44	0.41	0.38	0.35	0.29			
	0	0.50	0.48	0.45	0.43	0.39	0.35	0.21			
	0	0.50	0.48	0.45	0.42	0.37	0.34	0.24			
	0	0.48	0.45	0.44	0.42	0.37	0.34	0.24			
	0	0.46	0.44	0.43	0.41	0.35	0.32	0.25			
	0	0.49	0.44	0.43	0.40	0.34	0.30	0.19			
	0	0.52	0.48	0.44	0.41	0.39	0.36	0.29		36 hr	1.9
8	0	0.48	0.46	0.45	0.43	0.38	0.35	0.25		3 d	0.9
	0	0.48	0.46	0.44	0.43	0.38	0.35	0.28		4 d	0.4
	0	0.47	0.44	0.43	0.41	0.40	0.38	0.30		8 d	0.6
	0	0.48	0.46	0.44	0.43	0.39	0.35	0.28		9 d	1.0
	0	0.48	0.46	0.44	0.41	0.40	0.37	0.28		5 mo	1.0
	0	0.48	0.46	0.44	0.43	0.40	0.37	0.29			
	0	0.48	0.46	0.44	0.43	0.40	0.37	0.29			
	0	0.49	0.47	0.45	0.43	0.40	0.37	0.29			
9	+++	0.85	0.80	0.76	0.70	0.45	0.43	0.15			
10	0	0.45	0.44	0.42	0.40	0.39	0.33	0.29		4 d	1.2
	0	0.44	0.40	0.39	0.37	0.33	0.29	0.21			
	0	0.43	0.41	0.40	0.38	0.34	0.31	0.26			
11	0	0.48	0.45	0.43	0.42	0.38	0.34	0.29		1 1/2 hr	1.6
	0	0.50	0.47	0.45	0.43	0.38	0.35	0.29		4 d	1.3
	0	0.48	0.46	0.45	0.43	0.38	0.34	0.27		6 d	2.1
	0	0.48	0.44	0.43	0.40	0.37	0.33	0.27			
	0	0.43	0.41	0.40	0.39	0.34	0.31	0.24			
12	+	0.59	0.52	0.49	0.47	0.41	0.34	0.26		8 d	1.7
	+	0.63	0.55	0.51	0.50	0.44	0.41	0.34		70 d	1.6
	±	0.53	0.51	0.49	0.48	0.42	0.40	0.30			
	±	0.54	0.50	0.47	0.46	0.40	0.38	0.29			
	0	0.51	0.47	0.46	0.44	0.40	0.37	0.29			
	0	0.51	0.44	0.43	0.42	0.40	0.38	0.29			
13	0	0.49	0.47	0.45	0.43	0.39	0.36	0.24		1 hr	3.0
										26 d	0.6
14	+	0.71	0.63	0.47	0.43	0.38	0.35	0.32		1 1/2 hr	4.5
	+	0.68	0.57	0.45	0.42	0.38	0.35	0.29		3 1/2 hr	5.4
	±	0.59	0.46	0.43	0.40	0.37	0.34	0.28		4 hr	2.8
	±	0.59	0.46	0.43	0.42	0.37	0.34	0.29		6 hr	2.6
	±	0.59	0.46	0.43	0.41	0.37	0.34	0.29		7 hr	5.3
	0	0.52	0.48	0.45	0.44	0.39	0.35	0.25		14 hr	3.3
	0	0.52	0.47	0.45	0.44	0.39	0.35	0.25		17 1/2 hr	3.5
	0	0.49	0.46	0.44	0.43	0.40	0.37	0.29		17 hr	2.0
	0	0.48	0.44	0.43	0.42	0.37	0.35	0.26		2 d	0.7
	0	0.48	0.45	0.44	0.42	0.36	0.34	0.24		3 d	1.6
	0	0.45	0.43	0.41	0.40	0.35	0.32	0.25		4 d	1.5
	0	0.45	0.43	0.40	0.40	0.35	0.32	0.25		5 d	0.9
	0	0.48	0.46	0.44	0.43	0.37	0.34	0.29		6 d	0.7
	0	0.47	0.45	0.44	0.42	0.38	0.35	0.29			
	0	0.47	0.45	0.44	0.42	0.38	0.35	0.29			
	0	0.47	0.45	0.44	0.42	0.38	0.35	0.29			

TABLE 1 (continued).

CASE No.	URINALYSIS	HEMOGLOBINURIA	
		DEGREE IN URINE	KIDNEY FINDINGS AT AUTOPSY
1	10 hr.: red. 18 hr.: brown; hemoglobin,* 90 mg. per 100 cc.; pH 5.4; 130 cc.; specific gravity, 1.012; sediment—precipitate of hemoglobin, hemoglobin casts, trace of hemosiderin.	Severe	No autopsy
2	24 hr. (catheterized): dark brown; scanty amount; protein, +++; sediment—no red cells.	Severe	No autopsy
3	16 hr.: brown; pH 5.5; specific gravity, 1.022; protein, ++; sediment—innumerable hemoglobin casts, no red cells.	Moderate	No autopsy
4	16 hr.: dark red; hemoglobin,* 520 mg. per 100 cc.; pH 5.5; 265 cc.; specific gravity, 1.016; protein, +++; sediment—precipitate of hemoglobin, hemoglobin casts, hemosiderin ++. 46 hr.: light brown; hemoglobin,* 80 mg. per 100 cc.; pH 7.5; 40 cc.; specific gravity, 1.011; protein, +++; sediment—precipitate of hemoglobin, hemoglobin casts, hemosiderin ++.	Severe	Extensive hemoglobinuria; nephrosis.
5	17 hr.: dark red. 20 hr.: brown. 42 hr.: yellow; no hemoglobin; pH 5.8; 70 cc.; specific gravity, 1.014; protein +; sediment—no hemoglobin casts, hemosiderin +.	Moderate	Slight hemoglobinuria
6	24 hr.: black. 40 hr.: amber; no hemoglobin; pH 4.5; protein, ++; sediment—hemoglobin casts, hemosiderin ++.	Severe	Hemoglobinuria; interstitial nephritis; healing tubular nephritis.
7	16 hr.: dark brown; hemoglobin,* 80 mg. per 100 cc.; pH 5.1; 190 cc.; specific gravity, 1.010; protein, ++; sediment—precipitate of hemoglobin, hemoglobin casts, hemosiderin ++.	Severe	Slight hemoglobinuria; late tubular nephritis; slight interstitial nephritis.
8	13 hr.: dark red. 34 hr.: amber; trace of hemoglobin*; pH 5.8; protein, +, sediment—hemoglobin casts, hemosiderin +.	Severe	
9	2 hr. (catheterized): orange; trace of hemoglobin*; pH 5.5; 15 cc.; sediment—negative for hemoglobin casts, trace of hemosiderin, no red cells.	Slight	Slight hemoglobinuria
10	24 hr.: dark amber; trace of hemoglobin*; pH 7.0; 95 cc.; specific gravity, 1.010, protein, +++; sediment—no hemoglobin casts or hemosiderin. 44 hr.: orange, faint trace of hemoglobin*; pH 7.0; specific gravity, 1.008; protein, ++.	Slight	Hemoglobinuria; slight nephrosis and interstitial nephritis.
11	6 hr.: orange; questionable trace of hemoglobin; pH 7.0†; protein, +; sediment—no hemoglobin casts, no hemosiderin. 11 hr.: amber; negative for hemoglobin; pH 7.0; protein, ++; sediment—no hemoglobin casts, hemosiderin +.	None	No hemoglobinuria or renal abnormality
12	8 hr. (catheterized): yellow; no hemoglobin; pH 8.0†; 6 cc. 10 hr. (catheterized): amber; trace of hemoglobin; pH 7.0, 190 cc.; specific gravity, 1.015; protein, +++; sediment—no hemoglobin casts, no hemosiderin, many red cells.	None	No hemoglobinuria or renal abnormality
13	24 hr.: yellow; no hemoglobin; acid; 440 cc.; specific gravity, 1.020; protein, +; sediment—no casts. 48 hr.: red brown; acid; specific gravity, 1.022; 1020 cc.; sediment—many red cells and sulfadiazine crystals.	None	No hemoglobinuria or renal abnormality
14	4 hr.: yellow, no hemoglobin; acid†; 65 cc.; protein, +; sediment—no hemoglobin casts, hemosiderin +, few red cells (menstruation). 13 hr.: amber; trace of hemoglobin; slightly acid; protein, +++; sediment—no hemoglobin casts, hemosiderin ++, few red cells.	None	

*Positive reaction to benzidine; no red cells in sediment.

†Received intravenous sodium bicarbonate or sodium bicarbonate solution on both an admission and for 24 to 48 hours.

TABLE 1 (concluded).

CASE No.	VENOUS BLOOD			NONPROTEIN NITROGEN		SURFACE TREATMENT OF BURN	PLASMA ADMINISTERED		SULFONAMIDE THERAPY	RESPIRATORY COMPLICATIONS
	INTER-VAL AFTER BURN	HEM-ATOCRIT	HEMO-GLOBIN	INTER-VAL AFTER BURN	LEVEL		AMOUNT	INTER-VAL AFTER BURN		
	hr.	%	%		mg /100 cc.		units ¹	hr.		
1	20	39	90			Débridement, triple dye.	17	21	None	+++
2	14		111			Boric ointment, triple dye.	12	30	Sodium sulfadiazine, intravenous (begun at 27 hr.)	+++
3	13		130			Débridement, tannic acid and silver nitrate.	17	42	None	++++
	25		107							
	36	43	83							
4	16	47	105			Soap- and -water cleaning, boric ointment, tannic acid and silver nitrate.	26	39	Sodium sulfadiazine, intravenous (begun at 46 hr.)	++++
	36	43	96	36 hr.	87					
	60	37	84							
5	14		115	36 hr.	71	Soap- and -water cleaning, boric ointment, triple dye, tannic acid and silver nitrate.	13	40	Sulfadiazine, oral (begun at 36 hr.)	+++
	29		122							
	33		99	3 d.	48					
	41		100							
	59		88	4 d.	62					
6	40	42	90	64 hr.	56	Boric ointment, triple dye, sulfanilamide powder	30	48	Sodium sulfadiazine, intravenous (begun at 41 hr.)	+++
				3 d.	89					
	60	35	75	4 d.	95					
				5 d.	86					
				6 d.	92					
				7 d.	98					
7	23	46	115	36 hr.	48	Soap- and -water cleaning; triple dye.	11	24	Sodium sulfadiazine, intravenous (begun at 36 hr.)	++++
				3 d.	76					
	36	53	108	4 d.	63					
				5 d.	68					
	63	31	62	6 d.	76					
				7 d.	73					
				8 d.	71					
				9 d.	86					
				10 d.	65					
				11 d.	75					
				12 d.	75					
8	12	56	127	36 hr.	64	Boric ointment, triple dye	17	21	Sodium sulfadiazine intravenous (begun at 60 hr.)	+
				4 d.	42					
	36	53	111	5 d.	47					
				6 d.	37					
	64		92	8 d.	30					
				9 d.	33					
				11 d.	22					
				30 d.	17					
				3 mo.	18					
				5½ mo.	14					
9	2	45	109	2 hr.	36	None	9	4	Sodium sulfadiazine, intravenous (begun at 2½ hr.)	++++ (lobar pneumonia)
	3	40	97							
	4	35	82							
10	6	49	96	23 hr.	56	Débridement; tannic acid and silver nitrate; vaseline strips	9	12	None	0
	8	47	96	34 hr.	56					
	23		98	50 hr.	73					
	34	33	70	53 hr.	81					
	50	36	74	3 d.	90					
				4 d.	126					
11	2	45	95	2 hr.	31	Plaster cast on arms, vaseline dressings elsewhere.	20	43	Sulfadiazine oral (begun at 12 hr.)	+
	4	42	88	11 hr.	39					
	11	51	104	36 hr.	25					
	14	46	91	61 hr.	34					
	17	45	90	3 d.	25					
	25	42	84	4 d.	23					
	36	41	80	5 d.	44					
	61	42	78	7 d.	41					
				8 d.	84					
12	1	50	100	1 hr.	18	Débridement; triple dye	17	11	Sulfadiazine oral (begun at 4 d.)	0
	2	42	87	18 hr.	24					
	7	36	83	34 hr.	19					
	18	49	99	52 hr.	29					
	27	46	92	8 d.	14					
	34	43	80	16 d.	22					
	52	44	85	22 d.	29					
				27 d.	35					
13	1	43	90	1 hr.	19	Débridement; vaseline dressing on upper extremities, tannic acid and silver nitrate elsewhere	17	22	Sulfadiazine oral (begun at 10 hr.)	0
	4	43	87	13 hr.	40					
	7	45	95	24 hr.	49					
	13	62	125	36 hr.	59					
	17	61	124	60 hr.	32					
	18	42	99	4 d.	37					
	25	45	93	7 d.	34					
	38	55	113	11 d.	25					
	49	44	93	18 d.	29					
	60	43	88	30 d.	31					
14	1½	38	86	1½ hr.	25	Plaster cast on left arm, triple dye on thigh, bentonite (aluminum silicate) to left leg	6	5	Sodium sulfadiazine intravenous (begun at 12 hr.)	+
	2	39	87	14 hr.	35					
	7	37	71	18 hr.	51					
	14	44	101	62 hr.	41					
	38	39	82	3 d.	22					
	62	33	71	5 d.	25					
				11 d.	30					
				16 d.	31					
				23 d.	27					

¹One unit equals 250 cc.

Respiratory tract involvements graded as follows: slight (+); moderate (++); severe (+++); and very severe (++++).

ing problem presented by the many gravely ill patients. The urine data for Cases 1-8 in Table 1 are therefore necessarily incomplete concerning the total output of urine and the analysis of all specimens. In these cases one or more urine samples voided within sixteen to forty-two hours after the burn were examined critically. The pH and hemoglobin content were determined within a day after obtaining the specimen. Careful study of the sediment was not done until five days after collection of the early specimens, which were preserved in an icebox and remained acid and remarkably free from bacterial contamination. In the patients not injured at Cocoanut Grove (Cases 9-14), the collection and examination of urine was prompt and was more complete than in the Cocoanut Grove cases. Samples of venous blood were always examined within two hours after collection. The hematologic and chemical methods employed in this investigation have been described in detail in a previous paper.²⁰

Quantitative estimation of the *hemoglobin* in plasma and in urine was performed by the benzidine method of Bing and Baker.^{21, 22} Examination of *pigments* in plasma, serum or urine was made with the Hardy recording spectrophotometer.²³ The *pH* of urine was measured with a glass electrode. The *total protein* in urine, including hemoglobin and other proteins, was roughly estimated by observing the precipitate in a sample boiled after acidification with acetic acid. *Hemosiderin* was detected microscopically as black-staining particles in a drop of sediment from centrifuged urine observed after the addition of a drop of ammonium sulfide solution.²⁴ Blood samples were taken from the antecubital vein or femoral vein, using as anticoagulant a mixture of dry ammonium and potassium oxalate, 200 mg. per 100 cc. of blood.²⁵ The *hemoglobin* was determined by a photoelectric-cell colorimeter calibrated so that 100 per cent hemoglobin was equivalent to 15.6 gm. per 100 cc. The erythrocytic volume per cent or *hematocrit* was determined by the Wintrobe²⁶ method.

The number of unusually *spherical cells* present in the red-cell population was estimated from fixed smears of blood stained with Wright's stain. A cell was considered to be a spherocyte if it was small in diameter compared to the other red cells and was homogeneous and intensely stained. Using these crude criteria, several observers agreed within 0.5 to 1.0 per cent on the number of spherocytes in 1000 red cells counted if the number was 3 per cent or above. In smears from 16 normal subjects the number of red cells classified as spherocytes varied from zero to 0.4 per cent, with an average value of 0.2 per cent.

The *osmotic fragility* of red cells was determined from freshly drawn venous blood. Accurately measured 0.1-cc. samples of blood were pipetted into a series of tubes containing 1.0-cc. amounts of the following solutions: hypertonic sodium chloride (2.0, 1.5 and 1.0 per cent), isotonic sodium chloride (0.85 per cent), hypotonic sodium chloride (0.80 to 0.10 per cent) and distilled water. These reagents were maintained as stock solutions kept at room temperature. The samples were mixed and centrifuged, the supernatant fluid was poured into a separate set of clean tubes, and 0.5-cc. samples of the supernatant solutions were diluted to 10 cc. with distilled water in Evelyn colorimeter tubes. One drop of ammonium hydroxide was added to each tube, the sample mixed, and the hemoglobin determined in an Evelyn colorimeter

using filter No. 540. The colorimetric values observed in the hypertonic salt mixtures were averaged as the "blank" and subtracted from each value obtained in the hypotonic range to give a corrected figure for hemolysis. The percentage hemolysis at each salt concentration was then calculated by dividing the corrected figure for hemolysis by the similarly corrected figure for complete hemolysis produced in distilled water. The curve of osmotic fragility was next plotted, using the hemolysis in per cent on the ordinate and the corrected tonicity of the hypotonic mixture on the abscissa. Since the hypotonic mixtures contained 1.0 cc. of salt solution of known but different tonicities and 0.1 cc. of whole blood, the plasma contributed by the blood sample altered the final tonicity. Accordingly, the final tonicity of the hypotonic mixture was corrected assuming arbitrarily that the amount of plasma in each case was 55 per cent of the blood sample and that the plasma was osmotically equivalent to an 0.85 per

TABLE 2. *Normal Osmotic-Fragility Values Expressed as Tonicity of Sodium Chloride.*

DEGREE OF HEMOLYSIS	1%	2.5%	5%	10%	50%	75%	95%
Maximum	0.49	0.47	0.46	0.45	0.41	0.40	0.35
Minimum	0.42	0.40	0.38	0.37	0.33	0.31	0.21
Average	0.45	0.43	0.42	0.41	0.38	0.36	0.30

cent solution of sodium chloride. Table 2 shows the osmotic-fragility values for 30 normal subjects with hemoglobin levels of 80 to 105 per cent, comprising 13 males and 17 females between the ages of seventeen and sixty-one. There was no significant difference between males and females.

Autoagglutinins (cold agglutinins)²⁷ and *hemolysins*²⁸ were tested for in the serum from clotted venous blood samples. The serums were diluted serially with physiologic salt solution and to each dilution was added an equal volume of 2 per cent suspension of Group O erythrocytes. As a source of complement for the hemolysis tests fresh human serum was then added in quantities equal to the patient's serum. These mixtures were observed for agglutination or hemolysis after being chilled for one hour at 0°C. and again after subsequent incubation at 37.5°C for one hour.

HEMOGLOBINURIA

Observations were made on 40 patients with combined second-degree and third-degree thermal burns involving from 15 to 65 per cent of the body area. Eleven of these patients showed hemoglobinuria. The series includes 34 patients burned in the Cocoanut Grove disaster and 6 others. Detailed studies on 10 of the 11 patients showing hemoglobinuria (Cases 1-10) and on 4 patients showing no hemoglobinuria (Cases 11-14) are shown in Table 1. One patient with gross hemoglobinuria following a 65-per-cent burn sustained at Cocoanut Grove was omitted from the table because no determinations on the blood were made before death, which occurred in six hours. Gross hemoglobinuria was observed in 9 of 12 patients from Cocoanut Grove who showed combined second-degree and third-degree burns involving

*Observations made at the Massachusetts Institute of Technology

Histologic Examination of Kidneys

The kidneys were studied histologically in 9 patients.³⁵ In 3 patients (Cases 11, 12 and 13) who showed no hemoglobinuria there was no significant abnormality in the kidneys. In 6 patients (Cases 4, 5, 6, 7, 9 and 10) who showed hemoglobinuria the histology of the kidneys was consistent with that of hemoglobinuria, as evidenced by the finding of hemoglobin casts in the tubules in each case.

In general the histologic picture was as described below, with variations for particular patients, as indicated in Table 1. The casts in the tubules varied in number and appearance from typical hemoglobin casts to coarsely and finely granular, brownish or reddish casts. Some tubules also contained dense blue, hyaline material, occasionally polymorphonuclear leukocytes and mononuclear cells and, rarely, red cells. In some cases the epithelium of the tubules containing the hemoglobin casts showed evidence of degeneration and necrosis. The tubular epithelium was occasionally more granular than normal; in other cases there was evidence of regeneration of the epithelium of the tubules. In several cases the interstitial tissue showed areas of infiltration with lymphocytes, plasma cells and, rarely, eosinophils. In general the glomeruli and blood vessels were normal.

CHANGES IN RED CELLS

The osmotic fragility of the red cells was significantly increased above normal in 7 patients. Of these, 5 patients (Cases 1, 2, 4, 5 and 9) had hemoglobinuria and 2 patients (Cases 12 and 14) had no hemoglobinuria. No significant increase in osmotic fragility of the red cells was observed in 5 patients with hemoglobinuria (Cases 3, 6, 7, 8 and 10) and in 2 patients with no hemoglobinuria (Cases 11 and 13). It should be emphasized, however, that in 10 patients the earliest observation of the osmotic fragility was from seventeen to forty-four hours after the burn; the red cells in 6 of these 10 patients showed no significant elevation of the osmotic fragility. This interval was usually beyond the period of maximum hemoglobinuria and presumably, therefore, past the period of maximum blood destruction. The interval after the burn in which the initial observation was made of the osmotic fragility is shown in Figure 1. In 4 patients not from Cocanut Grove, the osmotic fragility of erythrocytes was determined promptly, within a period of a half to three hours after the burn. The fragility was normal in only 1 of these patients (Case 11), whose burn involved 20 per cent of the body area. In the other 3 patients, the osmotic fragility was increased as follows: slightly in Case 12, burned 65 per cent; moderately in Case

14, burned 15 per cent; and extremely in Case 9, burned 30 per cent. In the last case, hemoglobinuria was observed at a time when the osmotic

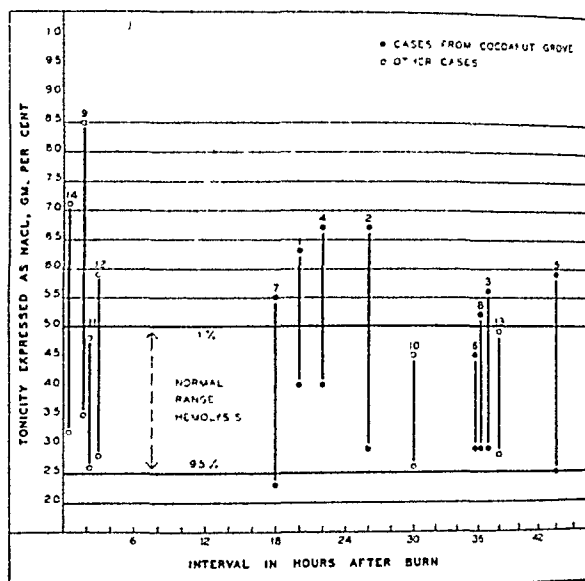


FIGURE 1. Relation of the Interval after the Burn to the Osmotic Fragility of the Red Cells.

The maximum range of osmotic fragility (from 1 to 95 per cent hemolysis) is shown for each of the 14 cases.

fragility test (Table 1 and Figure 2) indicated that 1 per cent of the patient's red cells were hemolyzed in isotonic (0.85 per cent) sodium chloride

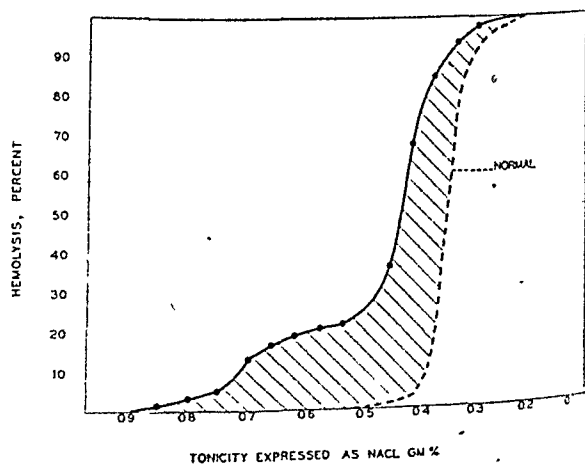


FIGURE 2. Curve of the Osmotic Fragility of the Red Cells from Case 9.

The cells were obtained two hours after a burn involving 30 per cent of the body, and three hours before the patient's death.

solution and thus, presumably, were susceptible to osmotic hemolysis in the patient's own isotonic blood plasma. The progressive disappearance and probable destruction of the red cells with abnormally increased osmotic fragility are shown for Cases 4 and 14 in Figures 3 and 4, respectively.

Blood smears from certain of the burned patients showed fragmentation, budding, spherocytes and microspherocytes of the red cells. Maximum fragmentation of red cells was seen only in the smears taken promptly after the burn, as in Case 14, shown in Figure 5. Deeply staining spherocytes

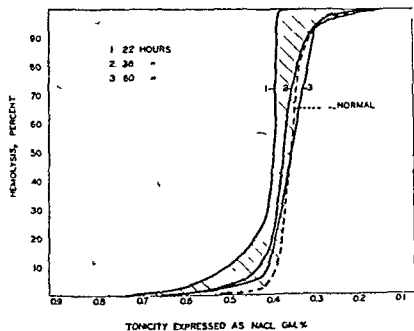


FIGURE 3. Serial Curves of the Osmotic Fragility of the Red Cells from Case 4.

This shows a progressive loss of abnormal cells up to sixty hours after the burn.

cytes, however, were detectable in significant numbers in Case 4 sixty hours after the burn, as shown in Figure 5. The spherocytes were observed to be significantly increased in number, being 3 per cent or above, in Cases 3, 4, 13 and 14, with simultaneous increases in osmotic fragility occurring in Cases 3, 4 and 14. In Case 13 the fragility was normal when determined thirty-eight hours after the burn, and accordingly the observation one hour after the burn of 3 per cent spherocytes in the blood smear constituted the only abnormality detected in the red cells. The disappearance of spherocytes from the blood smear coincident with the disappearance of red cells with increased osmotic fragility is shown in Figure 4.

Since autoagglutinins or autohemolysins might have arisen from the thermal burn and might have influenced the red cells, these antibodies were sought for in samples of blood serum obtained from Cases 1-8 seventeen to thirty-seven hours after the burn. No "cold" or "warm" agglutinins or hemolysins were detected in these samples taken at a time when increased osmotic fragility was observed in Cases 1, 2, 4 and 5.

EXPERIMENTAL STUDIES ON HEATED BLOOD

The experimental studies on human blood heated in vitro and on dog's blood heated in vitro and injected into the same animal are summarized briefly below and will be reported fully elsewhere

When samples of normal human defibrinated blood were heated in glass test tubes in a constant-temperature water bath to temperatures as high as 46°C. and the temperature was maintained constant for a period of one hour, no changes were observed in the erythrocytes. At temperatures of 47 to 50°C., abnormal changes in the red cells occurred depending on the duration of heating, which was extended to one hour as a maximum. Within a "critical zone" of temperatures (51 to 65°C.), abnormal changes always occurred even when blood samples were heated rapidly—in one

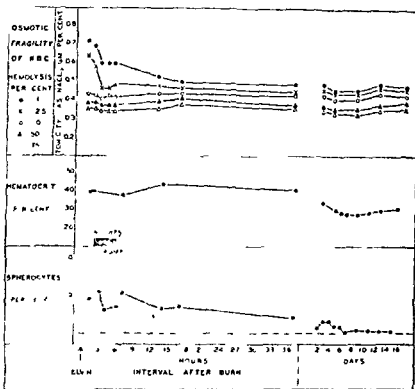


FIGURE 4. Progressive Loss of Spherocytes and of Red Cells of Increased Osmotic Fragility in Case 14.

and a half minutes—to a given temperature and immediately cooled to 37°C.

These abnormal or "thermal" changes in the red cells occurred in a regular and reproducible manner. The first detectable alteration was the formation of increasing numbers of rounded, budlike projections or filaments, at first connected with and finally disconnected from the erythrocytes. Progressive increase in this process of fragmentation was associated with the appearance of spherocytes, microspherocytes mixed with occasional "ghosts" and many erythrocytic fragments varying in diameter from 1 to 2 millimicrons down to innumerable small particles, approximately the size of bacteria, showing active brownian movement in a wet preparation. Coincident with the appearance of spherocytes and microspherocytes in the smear, the osmotic fragility of the red cells increased above normal and progressed to a maximum range with the progressive increase in spherocytosis of the erythrocytes. When the osmotic fragility increased to the maximum range, some of the red cells were susceptible to hemolysis as ob-

served in the fragility test in isotonic (0.85 per cent) sodium chloride solution. Hemolysis of the red cells varied with the temperature and with the duration of heating. The amount of hemolysis was negligible when the osmotic fragility was normal, when it was increased only moderately, and in many cases when it was increased to the maximum range. Temperatures of 55°C. or above pro-

fragility test and in vivo by injection of the heated blood into the same animal. None of the animals were burned. Five healthy dogs weighing from 12 to 18 kg. were bled of one sixth to one fourth of their blood, followed by the intravenous injection of an equal volume of isotonic sodium chloride solution containing 40 cc. of molar sodium lactate. In observations on dogs 1, 2 and 3, about

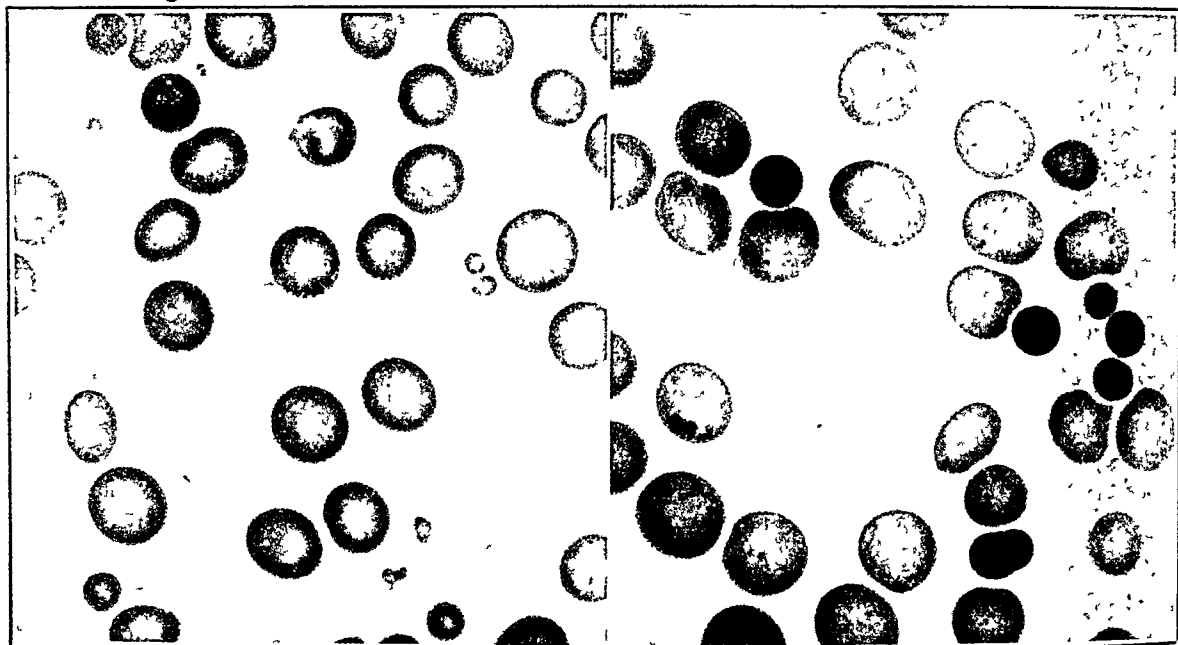


FIGURE 5. Stained Blood Smears after Burns ($\times 1000$).

The preparation on the left was made half an hour after the burn in Case 14; that on the right, sixty hours after the burn in Case 4. Both show densely stained spherocytes, and that on the left, a certain number of fragmented forms.

duced hemolysis that was progressive, ranging from 2 to 5 per cent of the red cells to complete hemolysis at 65°C. These thermal changes were inherent in the red cells themselves and did not depend on the medium in which they were suspended, whether plasma (heparinized), serum or isotonic salt solution, and were produced in vitro out of contact with the tissues. The serum from heated blood did not hemolyze or change normal red cells, and the serum from unheated blood did not reverse the changes in heated erythrocytes. When subjected to severe mechanical trauma for an hour in a test tube, blood that had previously been heated to 50°C., with a slight increase in osmotic fragility, showed no significant increase in susceptibility to hemolysis. However, after heating to 52, 55 and 58°C., respectively, the osmotic fragility and morphologic changes were maximal, and hemolysis from trauma increased progressively with the higher temperatures and was significantly greater than the hemolysis of blood heated to 50°C.

The susceptibility to hemolysis of heated blood from dogs was observed in vitro by the osmotic-

one fifth of each animal's blood volume was heated in vitro to approximately 53°C., producing maximum changes in morphology and in osmotic fragility, whether the red cells were heated in serum, washed and resuspended after heating in hypertonic (1.275 per cent) sodium chloride solution or washed and resuspended before heating in isotonic (0.85 per cent) sodium chloride solution. The heated suspension of red cells in each case was cooled to room temperature and injected into the same dog. Blood samples removed from these three animals immediately after injection showed an abnormal osmotic fragility comparable to the "mixed-population" fragility curves produced in vitro by mixing 20 to 30 per cent by volume of heated blood with unheated blood. The stained smear showed spherocytes immediately after injection. In the course of several hours after injection the spherocytes and abnormally fragile erythrocytes disappeared coincident with extreme hemoglobinemia and hemoglobinuria lasting for twenty-four to thirty-six hours. All three dogs recovered without reactions, without azotemia, and with the excretion of copious amounts of urine with a pH of

65 to 85°. As a control observation in dog 4, one fifth of the blood volume was removed, defibrinated, heated to 50°C., and reinjected. This degree of heat did not change the osmotic fragility of the red cells. Following injections there was no change in morphology or osmotic fragility, no disappearance of the animal's red cells and no hemoglobinuria. In a second control observation in dog 5, one fourth of the blood volume was removed into sodium citrate as an anticoagulant and heated to 53.7°C., and only the plasma, obtained by centrifugation, was reinjected. The heating produced a maximum increase in the osmotic fragility and considerable hemolysis of the red cells. Injection of the deep-red plasma, which was free of cells and fibrin, did not alter the osmotic fragility of the dog's red cells and produced only slight and transient hemoglobinemia and hemoglobinuria.

DISCUSSION

It is evident that hemoglobinuria as a complication of severe thermal burns results from the rapid destruction of red cells, producing hemoglobinemia with consequent excretion of free hemoglobin in the urine. Concerning the mechanism of hemolysis of red cells, no cold or warm agglutinins or hemolysins were found in samples of serum obtained from 4 patients at a time when their erythrocytes showed increased osmotic fragility. In 6 patients, the increased osmotic fragility occurred without or before sulfonamide therapy. In a patient (Case 9) whose osmotic fragility showed the greatest increase obtained in this series no chemicals were applied to the burn. There was no apparent clinical complication, such as pulmonary involvement, which was common to all cases either with hemoglobinuria or with increased osmotic fragility. All 14 patients received intravenous injections of large volumes of human plasma both with and without the development of hemoglobinuria or increased osmotic fragility. Other possible causes for destruction of erythrocytes may include intravascular thrombosis and possibly the formation of capillary emboli.³⁰

By contrast, the positive evidence derived from the observations of the patients and from the experiments reported here in brief form supports the belief that the principal and immediate cause of the increased blood destruction in thermal burns is the heating of the circulating blood in the tissues adjacent to the burned area. This evidence can be summarized as follows: The red cells from certain of the cases reported here, examined promptly after the burn, revealed a mixed population of normal cells and of spherocytes of varying sizes. The erythrocytes exhibited varying degrees of increased osmotic fragility. In severe cases of burn, heating of the tissues probably occurs, since subcutaneous

temperatures of from 51 to 65°C. have been produced and maintained for several minutes experimentally in anesthetized animals by scalding¹⁹ and by igniting turpentine on the skin.¹⁷ The heating of human blood *in vitro* within the critical zone of 51 to 65°C. produced irreversible and progressive fragmentation and formation of spherocytes, a progressive increase in the osmotic fragility in hypotonic salt solutions and hemolysis of some of the red cells in plasma, serum or isotonic salt solution. The effects produced by heat were inherent in the erythrocytes themselves and were not caused by demonstrable hemolytic agents or dependent on the presence of animal tissue, serum or plasma. The process of fragmentation apparently produced spherocytes and microspherocytes, possibly by removing from the erythrocyte a larger proportion of surface than of volume. If the usual osmotic properties of the surface and contents of the fragmented cells are retained, then from observations of Gänsslen,²⁷ Haden³⁸ and Castle and Daland,³⁹ spherocytes and microspherocytes will show an increase in osmotic fragility because their spheroidal shape permits less swelling before hemolysis occurs on reaching the spherical form, which is the form permitting no further increase in volume without increase in surface.

When the blood of dogs was heated sufficiently to cause increase in osmotic fragility and was then injected into the animal, presumably those red cells susceptible to hemolysis *in vitro* in isotonic sodium chloride solution were subject to osmotic hemolysis *in vivo* in the isotonic plasma of the animal. As for the less fragile erythrocytes susceptible to hemolysis only in hypotonic solutions, the mechanism of their destruction is probably analogous to that, for example, found in congenital hemolytic jaundice. As suggested by Ham and Castle,⁴⁰ cells that are not hemolyzed in isotonic salt solution or plasma may be slowly destroyed as a consequence of erythrocytosis in the spleen and other organs. Thus, it has been demonstrated by the above authors and by Tsai et al.^{41, 42} that the sterile incubation of normal human blood *in vitro* or the stagnation of animal blood *in vivo* leads to progressive increases in volume, spheroidicity and osmotic fragility such that eventually some of the cells are lysed in isotonic salt solution, plasma or serum. The possible influence of mechanical trauma as a cause of hemolysis requires further study.

In contrast with the observations on hemoglobinuria in dogs, in which the urine was copious and neutral or alkaline in reaction, kidney complications developed in certain of the burned patients who showed hemoglobinuria. Most of the severely burned patients, during the first twenty-four hours, showed oliguria, acid urine and albuminuria.

uria, but this triad did not appear to be associated with the development of chronic azotemia. Of 3 patients without hemoglobinuria, terminal azotemia occurred in 1 and transient azotemia in 2. Similar observations have been reported by Lucido⁴³ and by Cope and Rhinelander.⁷ When hemoglobinuria occurred with oliguria, however, chronic azotemia of moderate severity was observed in spite of re-establishment of adequate urine output in 4 of the 5 patients living more than five days. These were the only cases of chronic azotemia occurring in the 40 patients considered here whose burns involved from 15 to 65 per cent of the body area. This irreversible azotemia may represent a decrease in kidney function, but this cannot be established from the data available, especially in view of the large concentrations of nitrogen excreted in the urine, as reported by Taylor et al.³¹ Also, the azotemia might have regressed if these patients had lived longer than five to thirteen days and had recovered from their extensive burns. From the clinical observations, the use of triple dye in treatment of the burned area was not a factor common to the occurrence of chronic azotemia, since it was not used in 1 patient (Case 10) who showed this condition. Also triple dye was used in 1 patient (Case 8) who showed reversible azotemia. Large amounts of hemoglobin can be excreted by the human or animal kidney without azotemia if the urine is adequate in volume and neutral or alkaline in reaction.^{1, 2, 44} Hemoglobinuria^{44, 45} and methemoglobinuria⁴⁶ in animals excreting acid urine, however, have produced oliguria and uremia. In the patients considered here with irreversible azotemia, histologic examination of the kidneys post mortem revealed hemoglobin casts in each case, but there was no extensive obstruction of tubules by these casts or advanced changes in interstitial tissue or in tubular epithelium. The histologic changes did not explain adequately the apparent inability of the kidney to clear the blood normally of its content of nonprotein nitrogen products. The occurrence of azotemia together with hemoglobinuria in these patients is similar only in part to kidney complications following intravascular hemolysis from blackwater fever or transfusion of incompatible blood.^{44, 47} In these latter conditions the oliguria or anuria is usually protracted, resulting in higher degrees of azotemia, which may reverse completely with the re-establishment of diuresis. The mechanism of oliguria or anuria as related to the histology of the kidney in these conditions is a debated subject.^{44, 48, 49} The immediate treatment of a severely burned patient, however, should probably include the administration of fluids and

alkali in an attempt to establish prompt diuresis of neutral or alkaline urine.

In summary, it is probable that in thermal burns destruction of a considerable volume of erythrocytes may result directly from heating of blood at the site of the burn, depending on at least three major factors: the temperature attained by the blood, the duration of heating and the volume of blood subjected to these conditions. Accordingly, the thermal changes in blood may not correlate strictly with the area burned but may be anticipated in extensive third-degree burns. This concept possibly explains the high incidence of gross hemoglobinuria occurring in 9 out of 12 cases burned over a body area of 45 to 65 per cent in the Coconut Grove disaster. This fire may well have produced more intense and prolonged heating than did the source of burns in Cases 12 and 13, in which the patients were severely burned but showed no striking blood changes or hemoglobinuria.

The blood of burned patients, if examined early, may, as in this series, show alterations that vary from only slight spherocytosis of erythrocytes to advanced morphologic changes associated with an extreme increase in osmotic fragility involving 30 per cent of the patient's red cells, as indicated in Case 9 (Fig. 2). Correspondingly, blood destruction may be of a mild degree, as in Case 14 (Fig. 5), with no hemoglobinuria, or the rapid destruction of a considerable volume of red cells may be followed by hemoglobinemia, hemoglobinuria and possibly irreversible azotemia.

SUMMARY

Gross hemoglobinuria was observed in 9 cases and minimal hemoglobinuria in 2 among 40 cases receiving combined second-degree and third-degree thermal burns involving 15 to 65 per cent of the body area. The maximum excretion of hemoglobin occurred during the first twelve to twenty-four hours, then decreased rapidly.

The urine samples from patients with gross hemoglobinuria were scanty in amount for one or two days, varied from black to red to light brown, and were acid (pH 4.5 to 5.8), and the urines contained hemoglobin in solution, in precipitated form and in casts. The red and brown pigments were identified spectroscopically as oxyhemoglobin mixed with traces of methemoglobin. There was no evidence of myohemoglobin.

The plasma or serum from 8 cases showed hemoglobinemia. Spectroscopically, oxyhemoglobin and methemalbumin were detected in the serum examined from 1 patient.

Chronic azotemia of moderate severity occurred in spite of the re-establishment of adequate excre-

tion of urine in 4 of 5 patients with hemoglobinuria who lived five days or longer. In 6 patients with hemoglobinuria examined post mortem, the histology of the kidneys was consistent with hemoglobinuria in each case. It is suggested that the immediate treatment of severely burned patients should attempt to establish diuresis of alkaline urine.

No significant anemia developed in the first twenty-four to forty-eight hours in the 14 burned patients, of whom 10 showed hemoglobinuria.

If blood is rapidly heated to a temperature of 51 to 65°C, changes occur in the red cells consisting of fragmentation and the formation of spherocytes and microspherocytes, with a striking increase in osmotic fragility and hemolysis of the erythrocytes.

In patients with severe or moderately severe thermal burns, the red cells examined promptly after the burn exhibited changes in morphology and osmotic fragility similar to those obtained by the injection into dogs of the animals' own erythrocytes heated in vitro to approximately 53°C.

The increased osmotic fragility of heated red cells apparently results from conversion of the normal biconcave erythrocytes to more nearly spherical forms by a process of progressive fragmentation. The mechanism by which heat causes fragmentation of red cells is not defined. It is possible that destruction of the red cells with increased osmotic fragility in vitro occurred through a mechanism of swelling and osmotic hemolysis in the isotonic plasma of the animal.

In thermal burns a significant number of erythrocytes may be destroyed by heat, probably depending on the temperature attained by the blood, the duration of heating and the volume of blood subjected to these conditions.

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CLINICAL NOTE

PNEUMOCOCCAL MENINGITIS: RECOVERY FOLLOWING TREATMENT WITH SULFADIAZINE AND SPECIFIC ANTISERUM

REPORT OF A CASE

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BEFORE chemotherapy became of common use, only in isolated cases was there recovery from pneumococcal meningitis. Prior to the use of sulfonamides, mortalities as high as 95 to 100 per cent were reported. The few scattered recoveries reported may have been due to specific

116/74. There was a marked bulging of the right tympanum, marked rigidity of the neck and positive Kernig and Brudzinski signs. Paracentesis of the right ear revealed purulent exudate. An x-ray film of the right mastoid showed no evidence of an acute inflammatory process. The spinal fluid was under a pressure of 250 mm. The fluid was cloudy, and a pure culture of Type 5 pneumococcus was isolated. There were 360 cells per cubic millimeter—260 polymorphonuclear leukocytes and 100 lymphocytes. The protein was 192.5 mg. per 100 cc., the chlorides 643 mg., and the sugar 20 mg.

During the course of the illness four lumbar punctures were performed (Table 1). Because the patient appeared to improve clinically, these punctures were avoided as much as possible. An initial puncture was done to establish the diagnosis and to determine the etiologic agent. Owing to the presence of eye signs due to increased intracranial pressure, this procedure was repeated on the following day. Subsequent punctures were done to determine the progress of the case. As is evident from the table, the patient showed marked improvement in the 10-day period between the first and the last puncture.

Immediately after admission the patient was placed on a regimen of sulfadiazine, 45 gr. at once and 15 gr. every

TABLE 1. *Spinal-Fluid Findings.*

DATE	INITIAL PRESSURE	CHARACTER	CELL COUNT			SUGAR	PROTEIN	CHLORIDE	CULTURE
			TOTAL	LYMPHO- CYTES	POLY- MORPHO- NUCLEARS				
	mm. H ₂ O		per cu. mm.	per cu. mm.	per cu. mm.	mg./100 cc.	mg./100 cc.	mg./100 cc.	
8-24	250	Moderately cloudy	360	100	260	20	193	643	Type 5 pneumococcus
8-25	350	Moderately cloudy	310	120	190	27	103	650	Type 5 pneumococcus
8-27	110	Cloudy	—	—	—	—	—	—	—
9-3	126	Clear	27	18	9	45	35	680	No growth

antipneumococcus serum alone or may have been supplemented by various forms of drainage.¹ With the advent of the newer chemotherapeutic agents, the prognosis has been more promising.^{2,3} Some observers⁴⁻⁶ have found that serum used in combination with the sulfonamides has made the outlook even better than when either is used alone. It is the purpose of this paper to report a case of pneumococcal meningitis with recovery and to give in detail the plan of treatment followed.

CASE REPORT

S. G. A., a 12-year-old boy, entered the Pediatric Service of the Cambridge Hospital on August 24, 1942, in a semi-comatose condition. Four days previously, an upper respiratory infection had developed, followed by earache on the right side. Approximately 20 hours prior to admission he had headache, stiff neck, nausea and intermittent vomiting. The family history and past history were irrelevant.

On admission the temperature was 105.5°F., the pulse 130, and the respirations 30. The blood pressure was

4 hours thereafter. The initial dose was retained but subsequent doses were vomited. As a consequence, sodium sulfadiazine was given intravenously. Forty-five grains in 5 per cent glucose and saline solution was first administered, and this was followed 2 hours later by an intravenous injection of 30 gr. dissolved in 50 cc. of physiologic saline solution. The chemotherapeutic agent was then administered orally, in doses of 15 or 30 gr. every 4 to 6 hours. Concentrations of sulfadiazine in the blood were maintained in the vicinity of 20 mg. per 100 cc. On September 1, red cells began to appear in the urine, and medication was discontinued. The patient's general condition was considerably improved.

Since it was believed that combined drug-and-serum therapy would be of greater value than if either was used alone, the patient was simultaneously given Type 5 specific antipneumococcus serum, according to Table 2. Horse serum was first used, but this was changed to rabbit serum on noticing a mild chill following the second administration of horse serum. The administration of serum was continued until the quellung test on the serum had been positive on 3 successive days; a total of 930,000 units was given.

The patient responded promptly to therapy, and on the 3rd hospital day the temperature had fallen to normal. During the succeeding 9 days, however, it ranged from 100 to 102°F., becoming and remaining normal on and after the 12th hospital day.

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COMMENT

After the diagnosis of Type 5 pneumococcus meningitis was established by culturing the organisms from the spinal fluid, it was believed that

The tympanum of the right ear was incised on the day of admission and a purulent discharge was noticed. Culture from this exudate failed to reveal any pneumococcus organisms. This was, however,

TABLE 2 Dosage of Antipneumococcus Serum

DATE	TIME	DOSE OF HORSE SERUM		DOSE OF RABBIT SERUM		ROUTE	REACTION	REMARKS
		cc	units	cc	units			
8-24	6 00 p.m.							Horse serum eye sensitivity test negative
	6 30 p.m.	2	6 000			Intravenously	None	
	8 30 p.m.	8	24 000			Intravenously	Slight chill	
	11 45 p.m.							Rabbit serum eye sensitivity test negative
8-25	12 15 a.m.			2	8 000	Intravenously	None	
	1 30 a.m.			8	32 000	Intravenously	None	
	3 00 a.m.			10	40 000	Intravenously	None	
	4 30 a.m.			25	100 000	Intravenously	None	
	6 30 a.m.			15	60 000	Intravenously	None	
	11 00 a.m.			25	100 000	Intravenously	None	
	7 00 p.m.			25	100 000	Intravenously	None	
8-26	11 00 a.m.			25	100 000	Intravenously	None	
				25	100 000	Intramuscularly	None	Quelling test on serum negative
8-27	11 00 a.m.			25	100 000	Intramuscularly	None	Quelling test on serum positive
8-28	11 00 a.m.			25	100 000	Intramuscularly	None	Quelling test on serum positive
8-29	11 00 a.m.			15	60 000	Intramuscularly	None	Quelling test on serum positive

the case warranted the use of both sulfadiazine and specific antipneumococcus serum. As a result, the patient was given both forms of medication simultaneously. Because of his inability to retain the chemotherapeutic agent, the sodium salt of sulfadiazine was employed intravenously. Seventy-five grains of sodium sulfadiazine was thus used. This was followed by oral administration of the drug. At the same time specific antipneumococcus serum was given. The first ten doses were administered intravenously, and the remainder intramuscularly. During the first 24 hours, the patient received 670,000 units, consisting of 30,000 units from horse serum and 640,000 units from rabbit serum. A change to rabbit serum was made because of the apparent—though mild—chill reaction following the second dose of horse serum, because the prospect of large and repeated doses of serum would be required, and because it is thought by some that the rabbit serum antibody, being a smaller molecule than the horse serum antibody, may have a better penetrating action than the latter. Serum therapy was continued during the next 4 days by less frequent injections, mostly intramuscularly. A total of 930,000 units of Type 5 antipneumococcus serum was administered throughout the illness.

Apparently not a case of primary meningitis but one of meningitis secondary to otitis media. Frequent x-ray films of the right mastoid region were taken on the theory that if there was any evidence of an inflammatory condition, mastoidectomy with a view to wide drainage ought to be done immediately. The films showed no such inflammation at any time.

SUMMARY

A proved case of Type 5 pneumococcus meningitis with recovery is reported, with the plan of treatment outlined in detail. Both a chemotherapeutic agent and the specific antipneumococcus serum were employed. At no time did it appear advisable to institute mastoid surgery.

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MEDICAL PROGRESS

THE ANEMIAS OF PREGNANCY

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BOSTON

IN 1842, Channing¹ described a condition of severe anemia that occurred in the course of, and apparently as the result of, pregnancy. In 1919, Sir William Osler,² in a paper entitled "The Severe Anemia of Pregnancy," again drew attention to this condition and suggested that it had not received the study that it deserved. It is only during the last few years that any serious attempt has been made to classify the various anemias associated with pregnancy and to discover the factors that are responsible for the changes in the mechanics of blood manufacture and maintenance during this period. Despite the fact that a woman with anemia is inadequately fitted to the trials of labor, routine red-cell counts and hemoglobin determinations are too rarely done, either at antenatal clinics or in private practice.

Although pregnancy is a physiologic and normal condition that in a normal woman, provided an adequate and reasonable diet is taken, has no effect on the general health and no pathologic effect on the hematopoietic system, the requirements of the growing fetus, the alteration in maternal metabolism and the ordeal of labor, with its consequent blood loss, frequently cause anemia. Adair, Dieckmann and Grant,³ at the Chicago Lying-in Hospital, in a survey of 7835 patients, found that 63 per cent were anemic. Other American investigators—Lyon,⁴ Galloway⁵ and Moore⁶—with various methods of estimation, examined groups ranging from 100 to 1176 in number, and gave figures varying from 19 to 81 per cent of patients with less than 70 per cent hemoglobin. Various investigators have found this same condition in other countries.

Reid and Mackintosh⁷ investigated a group of 1108 pregnant women and found that 45.9 per cent gave a hemoglobin reading of 86 per cent or over, 43.9 per cent showed a reading between 70 and 84 per cent, and 10.2 per cent gave a reading of below 70 per cent. When the women were divided into two groups according to the family income, it was found that the incidence of anemia was considerably higher in the low-income group. The investigations of Bland, Goldstein and First⁸ showed the same thing. Multiparity in good financial cir-

cumstances does not appear to have much influence, except in women with five or more pregnancies, in which group the percentage with a hemoglobin reading below 70 per cent is three times as great as in those with fewer pregnancies. Age, work outside the home and abnormality in pregnancy have no demonstrable influence on the degree of anemia.

The anemias that are encountered in pregnancy fall into the following simple classification:

- A. Coexisting with, but unrelated to, pregnancy.
 1. Pernicious anemia, chronic chlorosis and leukemia.
 2. Anemias due to pre-existing chronic disease (namely, chronic nephritis).
- B. Anemias due to complications of pregnancy (namely, pyelonephritis, sepsis and bleeding).
- C. Anemias due to pregnancy.
 1. Physiologic anemia of pregnancy.
 2. Hypochromic anemia of pregnancy.
 3. Macrocytic anemia of pregnancy.

In this paper it is proposed to discuss only the anemias directly due to pregnancy.

PHYSIOLOGIC ANEMIA

The gravid state is commonly associated with important and well-marked changes in the circulatory mechanism. One of the most important physiologic alterations is an increase of blood volume. Dieckmann and Wegner⁹ determined the blood volume by the intravenous injection of vital red, and calculated the relative proportion of plasma and red cells by means of the hematocrit. These determinations were made on the same patients at intervals throughout pregnancy. The authors found an increase in plasma volume, total red cells and total hemoglobin, but since the increase in plasma volume is greater than the increase in the other two, although the actual number of circulating red cells and amount of hemoglobin are increased, the blood is more dilute. By ordinary methods of estimation there is, therefore, an apparent anemia affecting both the red cells and the hemoglobin. These are both proportionately reduced so that the color index remains at unity. By this means one can quite easily differentiate

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this condition from the iron-deficiency anemias, in which the color index is below 1.0.

Adamson and Smith¹⁰ in a study of 116 normal pregnant women found that during the second trimester there was a gradual drop in hemoglobin from an average of 76 to 68 per cent, and a drop in the red-cell count to 4,000,000. During the third trimester the hemoglobin continued at an average of 67 per cent, the red cells remaining about the same. In the two weeks following delivery, however, the blood rapidly returned to normal. Only 2 per cent of the patients continued through pregnancy without some drop in hemoglobin. Kühnel¹¹ in a carefully controlled study concluded that there is a gradual drop in the hemoglobin, cell volume and red-cell count until the sixteenth to the thirty-second week. This low level is maintained until about the thirtieth to the thirty-second week, when these substances begin to increase, but at thirty-four to thirty-six weeks a level is reached that is still lower than the initial one. Dieckmann and Wegner's¹² investigations showed an average decrease in the hemoglobin concentration amounting to 15 per cent at twenty-five to thirty-five weeks. From then on until term the hemoglobin increased and in many cases reached a normal level. At term the blood volume showed an average increase of 23 per cent, the plasma one of 25 per cent, and the total red-cell count one of 20 per cent, thus accounting for the decrease in hemoglobin concentration, cell volume and red-cell count seen in normal pregnancy. These authors demonstrated for the first time that although there are marked variations of all the indexes, especially of the color index, in the same patient, the average for each remains close to 1.0. The cell volume is slightly increased between the twenty-sixth and thirty-fifth weeks, when the physiologic anemia is most marked. The corpuscular hemoglobin is also slightly increased, both in amount and in percentage, but is normal at term. The means for the hemoglobin concentration in pregnancy are 11.56 gm. per 100 cc. of blood, for the cell volume 37.31 per cent, and for the red count 3,770,000. From these figures Dieckmann and Wegner conclude that the minimal standards for normal pregnancy are 10 gm. of hemoglobin, a hematocrit of 33 per cent and 3,360,000 red cells. Wintrobe¹³ in a careful study has shown that the lower limit of normal for the hemoglobin concentration in nonpregnant women is 13 gm. per 100 cc.

In the course of investigating blood volumes in many types of cases, Keith, Rowntree and Geraghty¹⁴ observed a post-partum decrease in total blood volume of approximately 1000 cc. They con-

sidered that only about 300 cc. of this could be accounted for in blood lost at the time of delivery. This observation also serves to explain, on the basis of dilution, the low hemoglobin before delivery and the relatively high estimations observed after it.

The smear shows no abnormality. There is no evidence of pathologic destruction of red cells, and nothing to suggest abnormal regeneration, such as nucleated red cells, polychromatophilia or reticulocytosis. The rise in blood values that occurs just after confinement cannot, therefore, be due to new blood formation.

This type of anemia is quite common, and does no apparent harm to mother or child. It entirely disappears during the first two post-partum weeks and, being physiologic, requires no treatment.

HYPOCHROMIC ANEMIA

Hypochromic, secondary or, as it is sometimes called, *microcytic anemia of pregnancy* occurs in women who have a subnormal hemoglobin in early pregnancy, and when the physiologic anemia develops, the drop in hemoglobin is so great that symptoms and signs of anemia occur; these may clear up or persist after delivery. Hypochromic anemia is extremely widespread, having been reported from all European countries, India and the Far East. It may occur with pregnancy at any age (Bland, Goldstein and First,⁸ Strauss and Castle¹⁵ and Mackay¹⁶).

In 1929, Lyon⁴ showed that over 30 per cent of pregnant women of the hospital class manifest some degree of hypochromic anemia, and Adair et al.³ found that 23 per cent of 1176 patients at the Chicago Lying-in Hospital had a hemoglobin of less than 10 gm. per 100 cc. Adair states that in Bengal nearly all the anemias of pregnancy are of the secondary type, and that the average hemoglobin of a native woman is about 50 per cent.³⁶

Although in a normal and robust woman the circulatory and hematopoietic adjustments in physiologic anemia as outlined above are sufficient to compensate for the demands of pregnancy, it is obvious that a woman who ordinarily maintains her full complement only with difficulty may, by reason of the pregnancy, easily become anemic. The fetus requires large quantities of maternal iron; the appetite, especially for iron-containing foods, may be capricious; the gastric function may be temporarily deranged; and any anemia that already exists is liable to exaggeration.

The mother has to supply the fetus, not only with sufficient iron to begin life, but also with sufficient store in the liver to carry it while on a diet consisting chiefly of milk, which is poor in

this mineral. The demand on the mother by the fetus for essentials of hematopoiesis has been likened to a chronic blood loss from other causes and represents a drain on the mother, especially during the latter part of pregnancy. The iron stores for the fetus must come either from the iron stores of the mother or from her food, according to Heath and Patek.¹⁷ They state that if 10 per cent reduction in hemoglobin results from hydremia, which may account for hemoglobin levels of about 70 per cent, a further reduction of 20 per cent, owing to demands of the fetus for iron, would reduce the hemoglobin to 50 per cent, assuming no stores or food source in the mother. There are said to be 500 mg. of iron in the average fetus (Sodeman¹⁸). Since the fetus requires more and more iron as it becomes larger, it is obvious that hypochromic anemia would tend to manifest itself or become definitely severe during the last three months of pregnancy. It is thus easy to see that this mineral drain by a ruthless intrauterine parasite may readily bring about an acute anemic breakdown in the mother, whose own reserves are thereby exhausted.

The maternal iron reserves are dependent on two factors, intake and absorption. If the intake is small, the maternal store may easily become depleted, and it is well known that a patient with the capricious appetite found commonly in pregnancy often does not relish the iron-containing foods. There is a widespread belief that meat is bad for pregnant women, and many women on their doctors' orders to take a diet throughout pregnancy that is deficient in essential factors, especially iron.

Impaired gastric secretion, leading to defective utilization of iron, appears to be a contributory factor. Strauss and Castle¹⁹ and Davies and Shelly²⁰ found that patients with hypochlorhydria or achlorhydria have a severer degree of anemia than do those with normal acid secretion. The anemia is typically hypochromic and microcytic. The hemoglobin is below 70 per cent and is commonly in the region of 50 per cent when advice is sought. The red cells usually number from 3,500,000 to 4,000,000 per cubic millimeter. The mean corpuscular volume, the mean corpuscular hemoglobin and the mean corpuscular hemoglobin concentration are all low. The leukocytes and platelets are unaffected. The red cells have a low mean diameter.

Strauss and Castle¹⁹ carefully followed during pregnancy 30 consecutive patients with uncomplicated hypochromic anemia whose hemoglobin and red-cell concentrations were less than half of normal. The chief presenting symptoms, appearing

usually at about midpregnancy or later, were a lack of sense of well-being and an excessive sense of fatigability. The average age of these patients was thirty-two years, and the average number of previous deliveries between five and six. In the severer cases pallor was observed. Atrophy of the papillae of the tongue was common. Brittle and suggestively spoon-shaped fingernails were seen in a few patients. Splenomegaly, disappearing with adequate treatment of the anemia, was observed in 4 cases. Achlorhydria persisting until after delivery was found in 17, hypochlorhydria in 10, and normal acidity of the gastric contents in only 2 of the 29 patients examined. The red-cell count of these women ranged from 2,120,000 to 4,830,000, and the hemoglobin from 25 to 44 per cent.

Patients do not die of this type of anemia. No knowledge of the post-mortem findings is therefore available, nor have biopsy examinations of the bone marrow been made.

Except in severe cases, the ultimate prognosis is good and labor is uneventful if there is no undue post-partum hemorrhage. The fetus itself is born with a normal red-cell count. In severe cases there may be great prostration with dyspnea and edema. Albuminuria may occur. The patients who are efficiently treated may go to term without difficulty and recover completely during the puerperium after a few weeks of iron treatment.

A regular rest period during the day should be insisted on. A full diet, including meat and fresh green vegetables, is important, although the appetite may require stimulation. The essential treatment is the taking of iron. There are many effective preparations available, but ferrous sulfate, 0.8 gm. daily, ferric ammonium citrate, 6 gm. daily, and Bland's pills, 4 gm. daily, are time-tested agents. Liver preparations have little or no effect on this form of anemia. Constipation should be corrected, provided treatment with iron does not eliminate this fault.

When hypochromic anemia is complicated by infection, a low basal metabolic rate, nitrogen retention or severe damage to vital organs, the effect of iron therapy may be disappointing, but the attempt should nevertheless be made.

MACROCYTIC ANEMIA

The macrocytic anemias of pregnancy constitute a much more dangerous complication than those of the iron-deficiency group, but are uncommon in this country. In the past the mortality rate was quite high, and it was probably this type that drew the attention of Channing in 1842 and Osler in 1919. With the development of modern methods and modern classifications, the macrocytic form of

anemia can now be clearly separated from the hypochromic anemia of pregnancy, and it is probable that the next few years will enable a proper estimate to be made of the true incidence of the former disease. Bardy,²¹ in 1924, reviewed 68 cases collected from the literature of Europe and America during a period of thirty-eight years. Esch,²² in 1921, was able to find only 23 cases in the German literature.

This anemia is often referred to as pernicious-like or pseudopernicious anemia of pregnancy to differentiate it from true pernicious anemia. In deed, the blood smear shows all the characteristics of pernicious anemia. Occasionally the differential diagnosis is difficult. Macrocytic anemia occurs in younger patients than does pernicious anemia, and usually develops during the last three months of gestation, but is often not recognized until shortly after delivery. Usually the pregnancy continues in a normal manner, with the patient becoming gradually paler or exhibiting a slightly jaundiced appearance, until the sixth or eighth month, when fainting, collapse, edema, albuminuria or excessive paleness may occur quite suddenly. In severe cases, edema and albuminuria give a clinical picture suggestive of nephritis, whereas coma may suggest toxemia. Syncopal attacks and retinal hemorrhage are not uncommon, but spinal-cord changes and glossitis do not arise. Rarely after the stress and shock of labor and delivery, the enfeebled patient suddenly collapses and becomes moribund. Premature labor is common, and the outlook for the infant is poor. Fever without demonstrable infection is not unusual, and when it occurs post partum may suggest puerperal sepsis. It disappears with anemia therapy. Retinal hemorrhages have been described by Hoskin and Ceiring-Cadle²³ and Cornell.²⁴ Gastrointestinal disturbances are of common occurrence.

Strauss and Castle¹⁹ found in a series of cases, that the red-cell count varied from 1,050,000 to 2,500,000 and the hemoglobin from 20 to 50 per cent (Sahli), resulting in a color index above 1.0. The red cells showed moderate variation in size and shape, with microcytes, occasional poikilocytes, oval macrocytes and rare megaloblasts. The leukocytes and platelets were either normal or slightly decreased. The mean corpuscular volume ranged from 105 to 130 cubic microns.

There is considerable disagreement concerning the question of recurrence in future pregnancies. Allan²⁵ does not consider that there is an association between the two. Reist,²⁶ on the other hand, says that the anemia, once established, tends to recur in subsequent pregnancies at an earlier date and to grow severer with each successive pregnan-

cy. This has also been stated by Vermelin and Vigneul²⁷ and Murdock.²⁸

The prognosis of both mother and child has been greatly improved in recent years owing to the development of blood transfusion and liver therapy. In untreated cases the mortality rate is high, being from 30 to 75 per cent for the mother and even higher for the infant. Cases that are treated early and energetically can safely be allowed to go to term. MacLeod and Wilson²⁹ describe a patient who was quite symptomless and uncomplaining until she suddenly collapsed and became moribund, and there are many other similar cases in the literature. Recovery is considerably retarded by sepsis. Most patients begin to recover with the birth of the child, and many have recovered spontaneously without treatment, once delivery is over. Soon after delivery there is usually a marked increase in reticulocytes.

The earlier writers called the macrocytic anemia of pregnancy "hemolytic anemia of pregnancy," but this term should be discarded because hemolysis is not a feature of the disease and is not caused by a hemolytic or toxic agent. Strauss and Castle¹⁹ have shown that the hematopoietic principle is probably deficient because of a temporary derangement of gastric secretion due to the pregnancy. The response of liver therapy is exactly the same as that found in true pernicious anemia, so that it is assumed that the anemia is due to the lack of hematopoietic principle. A deficiency in absorption may also be a factor.

Treatment consists in the administration of large doses of liver extract parenterally, and the response is as dramatic as in true pernicious anemia. Generally the use of liver preparations can be discontinued a few weeks after delivery, but it is well to maintain patients under observation, since it is possible for them subsequently to develop true pernicious anemia. If labor is not imminent, there will usually be sufficient recovery to allow of a normal labor without excessive danger or distress to the mother. Since there is frequently a partial deficiency of iron, it is well in addition to use iron in moderate dosage.

Patients who are desperately anemic or in whom infection is present and labor imminent should receive a blood transfusion, which may have to be repeated. Kersley and Mitchell³⁰ stress the value of transfusion in preventing obstetric shock in anemic patients. Matching of the blood for transfusion may be difficult owing to the factor of autoagglutination, which is sometimes present to a marked degree. Stewart and Harvy³¹ state that there is no difficulty if the test is performed at a temperature of 37°C.

In recent years, with the increasing popularity of blood transfusion as a therapeutic procedure, occasional cases are encountered of hemolytic reactions following the use of blood of the same group as that of the patient. These have been attributed to the presence of irregular isoantibodies in the patient's serum, but in all cases such antibodies were not demonstrable by cross-matching tests. New information on this point was obtained in 1940 when Landsteiner and Wiener³² detected a new factor in human blood (Rh) unrelated to agglutinogens A and B, and shortly thereafter Wiener and Peters³³ observed 3 cases of hemolytic reactions, 1 fatal, in which isoantibodies for this factor were present in the patients' serums. There were patients who had received previous transfusions, the anti-Rh isoantibodies being most likely the result of isoimmunization. Furthermore, it was found that transfusion accidents can occur at an initial transfusion owing to isoimmunization in pregnancy, the fetus in utero supplying the antigen (Wiener and Peters,³³ Levine and Stetson³⁴ and Levine, Katzin and Burnham³⁵). Some of these accidents had previously not been recognized as related to the transfusion but were believed to be merely pregnancy complications. Apparently the great majority of the reactions in repeated transfusions and in pregnancy cases are due to the Rh factor.

The condition is usually easily prevented by the optimal nutrition during pregnancy. The diet should contain adequate amounts of meat, eggs and whole-grain cereals.

* * *

During pregnancy, a mild type of anemia, physiologic in origin, is usually present. It does no apparent harm to mother or child and requires no treatment.

In this country, hypochromic anemia of a mild degree during pregnancy is not uncommon, and although seldom dangerous to life, is nevertheless responsible for minor ailments and ill health in both mother and child. It can readily be cured by iron therapy and a generous diet.

Occasionally anemia of a severe and dangerous type develops during and as a result of pregnancy. It demands detailed hematologic investigation and prompt treatment.

The hemoglobin level and of about the sixth month of an essential part of antenatal hematologic studies can then be carried

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**BENJAMIN CASTLEMAN, M.D., *Acting Editor*EDITH E. PARRIS, *Assistant Editor*

CASE 29441

PRESENTATION OF CASE

A thirty-eight-year-old man entered the hospital because of recurrent dyspnea of five years' duration.

Twenty-four years before entry, at the age of fourteen, the patient first noticed swelling in his neck. He was treated for several years by iodine and x-ray, without relief. At the age of twenty-one the right lobe of the thyroid gland was removed at an outside hospital. Following the operation he was told that he did not have a "toxic gland." The swelling and dysphagia, however, persisted. Five years later, at twenty-six years of age, the basal metabolic rate was said to have been normal and x-ray studies were said to have shown displacement of the trachea. He apparently received x-ray treatment and then was again operated on. There was a great deal of hemorrhage during the operation. Following the operation there was a persistent lump on the left side of the neck. Five years before entry he had a two-minute episode of dyspnea, during which he felt "strangled" and could not breathe in. Ten days before admission he had a similar episode while brushing his teeth. From both of these he recovered spontaneously. There had been no dysphagia, tremor or sweating. He had averaged 1 gr. of thyroid daily since the last operation.

An appendectomy had been performed two years before admission. One year later he had an attack of pain in the right flank and diarrhea.

Physical examination showed two transverse operative scars on the neck. Old x-ray changes were present in the skin over the suprasternal region, consisting of atrophy and multiple telangiectases. The left lobe of the thyroid gland was firm and measured 4 by 6 cm.; the isthmus was also palpable and firm. Examination was otherwise normal.

The blood pressure was 140 systolic, 90 diastolic. The temperature was 98.6°F, the pulse 70, and the respirations 22.

The blood showed a hemoglobin of 14.9 gm. and a white-cell count of 9100. The urine examination

*On leave of absence

was negative. The basal metabolic rate was +2 per cent.

An x-ray film of the chest showed a soft-tissue mass in the left side of the neck that displaced the trachea to the right and the esophagus posteriorly; no diverticulum was seen. The heart, lungs, aorta and diaphragm were normal.

On the fourth day a left thyroidectomy was performed under intratracheal nitrous oxide, oxygen and ether anesthesia. Considerable difficulty was encountered during the operation. The tissues seemed to be extremely vascular and densely adherent, without any planes of section. A lobulated mass, which in the upper portion measured 7 by 4 by 4 cm. and in the lower portion 5 by 4 by 4 cm., was finally removed. During the procedure the patient was carried under deep ether anesthesia, and at one time respirations had to be augmented by positive pressure to the bag, which was in the closed circuit. He received intravenous fluids and 500 cc. of whole blood. At the end of the operation his condition was fair. The systolic blood pressure was 60, and the pulse 120. On removal of the intratracheal tube, the airways remained clear. The blood pressure slowly rose with the patient in the shock position and continued intravenous fluids.

During the night of operation the systolic blood pressure was around 100, and the pulse 90 to 100. There was no evidence of hematoma in the neck, and only the usual moderate staining of the dressing. The patient remained in coma and twenty hours postoperatively had a right facial weakness. The pupils were moderately dilated and fixed. The corneal reflexes were absent. The blood pressure was 130 systolic, 80 diastolic. The pulse, which had been 80, increased to 100 but was regular. The temperature rose to 102°F. Twenty-four hours after operation he had an episode of projectile vomiting, following which the respirations became less frequent and more shallow. Although the air passages seemed clear, respirations finally ceased.

DIFFERENTIAL DIAGNOSIS

DR. J. H. MEANS: This seems to be a double header. I have to guess what kind of thyroid disease this patient had and also why he died.

Let us review a number of points that should be discussed. I am going to assume that the swelling of his neck at the age of fourteen was an enlarged thyroid gland. I have no adequate physical examination to permit me to make that statement flatly, but they say later on that they took out his thyroid, so I shall assume that it was thyroid. I might point out that there is no evidence in the story that the goiter was ever toxic. He was

treated, however, early in the course of the disease with iodine and x-ray without relief. That is not surprising because it does not sound like the kind of goiter that I should expect to be relieved by either of those procedures. The only goiters that I know of that are benefited by x-ray are toxic goiters, certain malignant goiters or that form of chronic thyroiditis known as lymphadenoid goiter or Hashimoto's struma.

I am interested in the fact that the patient had a great deal of hemorrhage from the second operation. Does that in any way have a bearing on the postoperative death at thirty-eight? I do not suppose it has, but it just passed through my mind that in women, sometimes after severe post-partum hemorrhage, the pituitary gland becomes infarcted and they develop *Simmonds's disease* later. I do not believe that anything of this sort occurred in this case, but I throw it out as something that might pass through one's mind in considering the case.

Even after the second operation the patient had a persistent lump in the left side of his neck. The episodes of dyspnea interest me. The caption at the top says that he came in for recurrent dyspnea of five years' duration. He had two attacks,—one at the beginning and the other at the end of this period,—which seems to me not exactly recurrent dyspnea of five years' duration. He did have two peculiar attacks that were characterized by dyspnea and a sense of strangling. That sounds to me like stridor of some sort rather than cardiac dyspnea or even asthma, although I suppose it could be.

He had received thyroid since his second operation. Why, I do not know. Nothing is stated to indicate that he was suffering from hypothyroidism. He had a good deal of the thyroid gland taken out, but we have no evidence on which to base a diagnosis of hypothyroidism.

We have to figure out what kind of goiter he had, and why he died. There are any quantity of things missing from this record that would be of diagnostic help to me. Perhaps to my later sorrow, I am going to throw out the pain in the right flank and the diarrhea as not bearing on the major issue.

This is a rather sketchy physical examination. There is no record of a Chvostek or Trousseau sign. I do know that when anyone gets a history of stridor after two thyroidectomies, one certainly would want to look at the vocal cords; but there is no mention of that either. I should like a better examination of the neck. They say that the thyroid gland was firm and that they felt the isthmus. I would want to know about the consistence and the surface, whether it was adherent to anything,

or if there were any palpable lymph nodes. Since they state that it was "otherwise negative," I shall assume that no lymph nodes were felt.

The x-ray examination disclosed a goiter in his neck, but, not in his chest, which pushed the trachea to the right and the esophagus backward. It would be disconcerting if this turned out to be not a goiter at all but some other cervical tumor. I should also like to know whether it went up or down when he swallowed. Maybe they did not try that.

DR. BENJAMIN CASTLEMAN: You have everything that is in the record, Dr. Means. I suppose the scantiness of the record is due to the fact that the patient was in the private pavilion of the hospital.

DR. MEANS: We know that the trachea and esophagus were compressed. Therefore, they did a thyroidectomy. That is right and proper. What are the indications for thyroidectomy in general? Thyrotoxicosis, under certain circumstances but not always, the production of pressure, and the suspicion of malignancy or the knowledge that it is malignant. I suspect they took out this goiter because of pressure. They may have thought it was malignant, or even that it was a constricting thyroiditis.

What kind of goiter did they take out? I do not believe that the patient had hyperplastic or simple colloid goiter. The general course and the chronicity of this disease are consistent with an old, nodular, partly adenomatous, partly cystic goiter. I cannot say that it is not some form of chronic thyroiditis, like Riedel's struma. On the other hand, I cannot say that it is, because we do not have the information. It could be a lymphadenoid goiter, but I do not believe that it was. He may have had an adenomatous or a cystadenomatous goiter for a great many years and had a malignant change in it. It would be impossible for me to say. Sometimes even the pathologist has difficulty in determining whether a goiter is malignant.

The next thing that intrigues me is the difficulty that the surgeons had at the time of operation. From the description it was difficult to remove this goiter. In fact the patient did not survive! We are told that the tissues seemed to be extremely vascular and closely adherent, without any planes of section. Does that tell us anything about the pathology of the goiter? Not a great deal, because of what had been done to it. The goiter had been subjected to enough heavy radiation to give telangiectases. We used to be told by surgeons that prolonged x-ray treatment did just this. The surgeons had difficulty in operating because the goiters were extremely adherent and vascular; indeed, just like this one. The x-ray treatment

may have contributed something, although I do not blame it for everything. If they had had a bad time twice before, one would expect the cleavage planes to be gone. They had a bad time with the anesthesia. I do not mean to say that it was not excellent anesthesia, but the patient did not do well under it. I am very much intrigued with the statement about deep anesthesia. I am also interested in the fact that the respirations had to be augmented by positive pressure; they practically had to give artificial respiration. The blood pressure faded out, and they had to give the patient a lot of fluid. Maybe they gave too much.

There was a severe degree of anoxia during the operation, and although I am not certain, possibly a brain injury was sustained during the operation that was irreversible. There is a queer statement that I cannot figure out. After transfusion they say that the patient's condition was fair, and later, that he remained in coma. When did he go into coma? Did he ever come out of anesthesia?

DR. CASTLEMAN: No.

DR. MEANS: The terminal event is strongly suggestive of something intracranial. We have no examination of the fundi. We have no complete neurologic examination. We do not know whether the facial palsy was central or peripheral in type. The patient probably had increased intracranial pressure just in the hours before death, and that may be what killed him. There is no mention of a lumbar puncture.

Why did he die? I should like to suggest as a possible cause for death that he had hypoparathyroidism, and that he had had it since after the first operation, — or more likely since the second which was on the other side, — not complete but low grade. That could have caused these two attacks of stridor, and it may be that they did not know he had it when they anesthetized him. At least there is no mention of any blood chemical studies. He may have had a low blood calcium plus anoxemia, and he may have gone into a state from which he could not recover, chiefly one of brain injury due to anoxia. He had no stridor, — at least we do not know that he did, — just difficult breathing.

I posted myself a little bit on hypoparathyroidism, the effect of low calcium and so forth, and found that one can get a number of cerebral manifestations in that condition. In one case in Dr. Albright's published series,¹ there was stiffness of the right arm and leg, and partial hemiplegia. Papilledema has been described, and I therefore think that hypoparathyroidism plus anesthesia might have accounted for death. Indeed, that is my first choice, although a risky one.

The patient may have had palsy of the vocal cords. If he had had an abductor paralysis and stridor, they would have inserted a tracheotomy tube. I am interested in all this intravenous fluid they gave because if they thought he had increased intracranial pressure they would not have given the fluid. The signs of intracranial pressure appeared, and no doubt this contributed to his death.

He may have had metastases from a malignant thyroid gland. The metastatic properties of the thyroid are bizarre. I can conceive of a solitary metastasis with hemorrhage from it; but there is no way of proving that and I think that it is unlikely. He may have had hypoparathyroidism, however. They could have removed too much of the parathyroid tissue at the first or second operation.

Did he have a mediastinal mass of any kind?

DR. GEORGE W. HOLMES: I should say that the lungs and mediastinum are absolutely normal. In the lateral view the trachea does not seem to be narrow or displaced. So far as I can make out, there is nothing to cause pressure on the trachea. One other possibility is that in certain cases with heavy x-ray treatment, the trachea collapses like a bag, due to absorption of the cartilaginous ring.

DR. MEANS: I had thought of collapse, but in the record it said that the airways were perfectly good. I therefore thought that the trachea had not collapsed.

DR. JULIA ARROWOOD: The mere fact that the patient had to have artificial respiration with bag and oxygen does not necessarily mean he had anoxia — in fact, quite the contrary. He had an endotracheal tube in place and could be perfectly well oxygenated even though he was not breathing for a time.

DR. WYMAN RICHARDSON: Did he have any preoperative medication?

DR. CASTLEMAN: That morning he had $1\frac{1}{2}$ gr. of Nembutal at 9:00 and $\frac{1}{4}$ gr. of morphine and $1/100$ gr. of atropine at 11:00.

DR. ARROWOOD: Again, in cases of cerebral anoxia one would expect a higher temperature than 102°F. and would not expect localizing signs on the right. Convulsions do not always occur. In 26 cases of cerebral anoxia reported by Courville² there was some type of muscular manifestations in all except those who died within a short time after operation.

DR. MEANS: The patient could have subarachnoid hemorrhage for all I know, but there is no neurologic evidence for it. He could have had some kind of apoplexy. He was only thirty-eight years old. Cerebral accident is a possibility.

DR. CASTLEMAN: Such as what?

DR. MEANS: Hemorrhage, either subarachnoid or ordinary cerebral hemorrhage, or thrombosis. It is all guesswork with this scanty evidence.

CLINICAL DIAGNOSES

Recurrent adenoma of thyroid.
Postoperative cerebral anoxia.

DR. MEANS'S DIAGNOSES

Nontoxic nodular goiter, adenomatous.
Postoperative cerebral anoxia.
Hypoparathyroidism?
Cerebral vascular accident?

ANATOMICAL DIAGNOSES

Multiple fetal adenomas of thyroid, with carcinomatous change in one.
Operative wound, recent: left thyroidectomy.
Cerebral embolus, left middle cerebral artery.
Cerebral infarct.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The surgical specimen removed was a nodular goiter that on section showed reddish to orange-brown nodules rather characteristic of what is known as fetal adenoma. One of these showed definite evidence of malignancy, but there were no metastases. The cause of death was cerebral, and Dr. Kubik will tell us about that.

DR. CHARLES S. KUBIK: There was an embolus in the left middle cerebral artery, with infarction of the brain in the distribution of the occluded artery. There were no thrombi in the heart to serve as a source for the embolus. Anomalous thyroid arteries are sometimes given off from the common carotid, proximal to the origin of the external carotid artery, and it seems reasonable to suppose that a clot might have been dislodged from such an anomalous vessel into the common carotid and might have been carried into the internal carotid and thence into the brain. The fact that the embolus was on the same side as the operation fits in with this theory. Microscopically the embolus consisted of very recent blood clot in which there was no organization.

DR. MEANS: Did you find any parathyroid glands?

DR. CASTLEMAN: No. The operative field was so scarred because of the previous operations and the x-ray treatment that we could not find anything that could be identified as a parathyroid gland. We cannot rule out Dr. Means's hypothesis that the patient had hypoparathyroidism, but there is no doubt that the cause of death was a cerebral embolus.

DR. MEANS: One has to explain the symptoms. It was suggested that the patient came in with recurrent attacks of dyspnea. They remain explainable unless the goiter caused them. They may have undergone some rapid enlargement on these occasions, with hemorrhage into a cyst. Do you find a cyst?

DR. CASTLEMAN: No.

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CASE 29442

PRESENTATION OF CASE

First admission. An eleven-year-old boy entered the hospital because of abdominal pain of six days duration.

The patient had had measles, chicken pox and scarlet fever during his earlier life, but had been in generally good health until the age of eight. From this time on, he had numerous episodes of abdominal pain, diarrhea and vomiting. He appeared to tire easily and seemed unable to keep up with the other children. In general, however, he was in fairly good health. Six days before entry, while at a Boy Scout camp, he developed low midabdominal pain, which was present on waking and sometimes went away in one or two hours. The pain continued intermittently until the day of admission. For the two days before entry, he had had frequent attacks of vomiting, as well as diarrhea consisting of eight or nine nonbloody nonmucous stools daily. The day of admission the abdominal pain became constant and he had three bowel movements. There were no urinary symptoms, chills, fever or jaundice.

Physical examination showed a well-developed and well-nourished boy with a somewhat anxious expression. The heart and lungs were normal. The abdomen was flat but a dilated loop of bowel transiently appearing at the level of the umbilicus was seen by two observers. No masses were palpable. There was no spasm, but tenderness and rebound tenderness were present in the right lower quadrant and also referred there from other parts of the abdomen. The right testicle was not located; the left was small and high in the scrotum. Rectal examination revealed tenderness on the right.

The temperature was 98.8°F., the pulse 80, and the respirations 22.

The urine was negative. The white-cell count was 17,000. A blood Hinton test was negative. A plain x-ray film of the abdomen showed

evidence of intestinal obstruction. A loop of gas-filled intestine, probably sigmoid, was seen superimposed upon the pelvis.

Ten hours after admission an appendectomy was performed through a pararectus incision. The appendix appeared grossly normal. The mesenteric lymph nodes were moderately enlarged. The cecum was fairly long and minimally inflamed. The terminal ileum was normal. There was no Meckel's diverticulum. The pathological diagnosis was "healing appendix." The postoperative diagnosis was mesenteric adenitis. He was discharged on the eighth hospital day.

Second admission (two weeks later). After discharge the boy remained well for the first three days, following which he began having sharp, crampy pains across the middle of the abdomen. The attacks lasted a few seconds, with intervals of about five minutes between the attacks. The pain became progressively severer and more painful so that he doubled up with the attacks and stayed awake at night. There were two episodes of vomiting, one occurring ten days and one eleven days before re-admission. During the attacks of pain the abdomen became distended, but the distention disappeared between the attacks. The abdomen, however, became more distended during the second week. He had alternating constipation and diarrhea. In the fifteen hours before entry he had two loose bowel movements. He was seen by his physician, who observed that during the attacks of abdominal pain there were audible peristalsis and definite coils of intestine moving against the abdominal wall. He was given belladonna without relief.

Physical examination showed a greatly distended abdomen, with marked tenderness but no spasm. Moderately high-pitched peristalsis was audible. There was some tenderness in the line of the incision, which was well healed. Rectal examination revealed mild tenderness high on the right, but only slight induration; the examination was otherwise not remarkable.

The blood pressure was 110 systolic, 70 diastolic. The temperature was 101°F, the pulse 110, and the respirations 22.

The urine showed a specific gravity of 1.025; the sediment contained 1 red cell and 2 white cells per high-power field. The red cell count was 5,460,000, with a hemoglobin of 100 per cent. The white-cell count was 9800, with 49 per cent neutrophils, which showed moderate toxic granulation. The stools were guaiac negative; and culture yielded no pathogens. The blood protein was 7.2 gm. per 100 cc, and the chloride 99.8 milliequiv. per liter. A Miller-Abbott tube passed with some initial difficulty to the upper jejunum

and considerably relieved the distention. He received a 400-cc. whole-blood transfusion and daily intravenous fluid.

On the second hospital day he had two bowel movements and was quite comfortable. At that



FIGURE 1. Opaque Enema Showing Obstruction of the Colon by a Mass (arrows) below the Splenic Flexure

Note the flecks of bismuth in the dilated colon above the obstruction.

time peristalsis was very active but "not obstructive." There was slight, constant tenderness below and to the left of the umbilicus, with rebound tenderness referred to the point of pressure. A plain film of the abdomen showed a loop of dilated small bowel in the right upper quadrant. There was gas within the colon. The right side of the colon contained flecks of opaque material, apparently representing bismuth. One day later the opaque material had moved to the region of the splenic flexure. At that time the tip of the Miller-Abbott tube was at the ileocecal valve, and the small intestine was deflated. An intravenous pyelogram was negative.

On the third day the boy vomited 50 cc. of fluid and had two loose bowel movements. The Miller-Abbott tube was draining fecal material, which frequently plugged the tube. He was not distended. The temperature was 100.5°F, and the pulse about 100. On the fifth day the temperature rose to 103°F. He had crampy abdominal pains, vomited once and had one bowel movement. One hundred cubic centimeters of stomach contents was aspirated with apparent relief.

A plain film of the abdomen showed the Miller-Abbott tube to be in the third jejunal loop. In

the left upper quadrant there seemed to be a mass pressing the colon laterally and deforming it. Neither the left kidney shadow nor the psoas contour could be made out. Some indefinite motting was seen in this area, which could have been in the large distended colon or in the mass. One dilated loop of fluid-filled bowel was present, but it was impossible to say whether this was large or small intestine. There were several loops of small bowel that contained gas but were not greatly dilated. A barium enema showed the opaque material to pass quite readily to the proximal descending colon, where an obstruction was encountered. The colon was compressed laterally against the abdominal wall, and there was a defect medially about 5 cm. long, over which the bowel was ragged and irregular. On one film there appeared to be an annular constriction which, however, was not seen on a subsequent examination.

An abdominal exploration was performed on the seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. OLIVER COPE: The record evidently does not give the confusion that the clinical picture did at the time; to me the record on certain points is clear. I am struck by the fact that an intravenous pyelogram was done. At the second admission the kidney was again investigated. I wonder why so much attention was given to the kidney.

The child suffered from intermittent intestinal obstruction—that much seems to be clear. The second point that is clear is that the appendectomy did not cure him, in other words, the disease was not appendicitis. The third feature is that the correct diagnosis was not made at the time of the first operation. Perhaps the operator observed more than is given in the record, but one thing is important—namely, that he noted minimal inflammation of the cecum. Such inflammation in the presence of a normal appendix and signs of intermittent intestinal obstruction perhaps should have been diagnostic. It is difficult to be sure but it is possible that the surgeon who operated on the patient at the first operation failed to make a diagnosis when he could have. The other thing that the surgeon should have noted, if possible, having observed inflammation of the cecum and a normal appendix, is whether the cecum was attached by a loose mesentery. I get the impression that the cecum was fairly long. We ought to have a more accurate description of that in anatomic terms. I suppose it means that the cecum was on a loose mesentery. In addition we should have been informed whether the large bowel was

palpated and whether it was properly rotated. If a segment of large bowel had an ample mesentery it suggests that rotation may not have been complete.

After the first operation intermittent obstruction recurred, and the episodes on the second admission sound to me like obstruction, with beginning impairment of circulation of part of the bowel, causing a rise in temperature and an increase in the illness of the patient. The diarrhea fits with such a point of view. It is interesting that there was no blood in the stools.

DR. BENJAMIN CASTLEMAN: One out of four stool examinations showed a ++ guaiac test.

DR. COPE: That is reasonable. It would be unusual, I believe, for intussusception to exist as long as the final episode did without some blood in the stools. There are two diagnoses in my mind that fit the entire picture. The commonest one is intussusception. Although the x-ray picture is consistent, perhaps we should get the details from the X-ray Department before being too flat-footed about it. It would be unusual, however, not to find a mass palpable in the abdomen if the intussusception started at the ileocecal valve and telescoped enough of the large bowel to bring the mass into the left upper quadrant. The X-ray Department found a mass, but it was not felt on physical examination.

The other diagnosis that I think is the only other plausible one—perhaps I am being far too hasty—is torsion of a partially rotated large intestine. The x-ray examination suggests at one place that there is a large gas-filled loop, which is the usual accompaniment of torsion. Torsion is a less likely diagnosis than intussusception but one that could occur and cause obstruction at the splenic flexure. Both these lesions may form and relieve themselves and therefore may recur intermittently. It is only when the intussusception becomes advanced enough so that it cannot reduce itself, or when the torsion has been present for some time, that impairment of the bowel wall occurs.

DR. MILFORD SCHULZ: In the barium enema you can see an obstruction just below the splenic flexure. The colon is displaced laterally against the abdominal wall, and there is a constant defect, which is 5 or 6 cm. in length. The defect is not suggestive of an intussusception, since you can see fairly distended colon just above the area of obstruction, visualized by the bismuth that had previously been given as medication. Here is the annular constriction. Here it is on another examination. Something is fixed to the soft tissues, displacing the colon laterally. The impression at the time of examination was that it should have been a carcinoma, but in view of the boy's age a

compromise diagnosis of either lymphoma or an inflammatory lesion was suggested. The pyelogram was done because of the possibility of a retroperitoneal inflammatory process.

DR. COPE: The x-ray films are impressive. When I read the record I did not get the slant that I do now from your recounting and pointing out the characteristics of a malignant tumor. The thing that may be the red herring is the observation of inflammation of the cecum at the first operation. Such inflammation should mean either *torsion* or *intussusception* that had relieved itself.

Could an intrinsic lesion of the bowel explain the x-ray findings?

DR. SCHULZ: Yes, I think it could.

DR. COPE: May I ask for the confines of the mass described? Could it be accounted for by inflammation outside the splenic flexure?

DR. SCHULZ: Here you see the mass in the left upper quadrant with some mottling within it. It may be a distended colon with gas and fecal material, or it may all be extrinsic to the colon, perhaps with some necrotic material within it. I might say in passing that the x-ray appearance of intussusception is usually quite characteristic.

DR. COPE: Intussusception may result from a tumor so that the obstruction of the bowel becomes complete only when intussusception occurs. There is nothing in the history that excludes the presence of a large polyp or tumor that gave some mechanical difficulty resulting eventually in obstruction. The patient certainly had intestinal obstruction. We have some evidence of a mass or tumor by x-ray, which, if that were the primary agent of the obstruction, ought to have resulted, not in intermittent obstruction, but in permanent obstruction. It is possible that the episodes before the first operation were the initial phase of obstruction, over a period of months, and resulted in final obstruction at the time of the second admission. I am still impressed by the story of the intermittent character as it is given in the record and by the fact that the boy was apparently relieved of obstruction at the time of the first operation. Therefore, I shall stick to the idea of either intussusception or a volvulus of the large intestine in the absence of more positive evidence of intrinsic tumor. In the absence of the positive x-ray finding of intussusception, I am inclined, leaning heavily on the "loose" cecum, to make a diagnosis of volvulus of the large bowel with some degree of necrosis, possibly going on to abscess formation to account for the x-ray finding.

DR. SCHULZ: Does not a loop of bowel with volvulus usually contain a lot of gas?

DR. COPE: That is true. The two cases of volvulus of the right side of the colon that I remember vividly both had a big bolus of gas in the cecum. That was not found here, but in neither of my cases had the bowel been decompressed from above by a Miller-Abbott tube. We have evidence from the history that the Miller-Abbott tube had decompressed the small and large bowels, and fecal material had drained through the tube. So one would not necessarily expect to find a distended bowel proximally.

DR. ROBERT R. LINTON: How often does volvulus occur in a child of eleven? Volvulus of the large bowel has always occurred in older patients as I remember it.

DR. COPE: Some of the house staff may remember a physician who, at the age of thirty, had a volvulus of the right side of the colon. He had undoubtedly had intermittent attacks of the volvulus since the age of six. After one, the appendix had been removed. The story was much like this one only it lasted over a period of many more years. The doctor's father told me that when the attacks occurred in childhood, the boy would get down on his hands and knees suffering from intense colic and try to defecate. After an hour or two of rolling around the attack would be relieved. When he first came to us the attack had lasted three days—much longer than any previous attack. He had a volvulus with gangrene of the bowel and had a stormy time from generalized peritonitis. If one makes a diagnosis of volvulus in this boy, one has to assume that there was necrosis of the bowel to account for the increasing septic appearance of the chart and also for the x-ray findings.

DR. CASTLEMAN: If volvulus had been present all this time, do you not think that it would have been seen at the first operation?

DR. COPE: Volvulus could not have been present all this time. It would have to have been intermittent. The patients I have seen with intermittent volvulus or intussusception have had appendectomies following an attack and the correct diagnosis was not made at the first operation. I imagine it may be a difficult thing to recognize.

DR. FRANCIS MOORE: The surgeon who performed the first operation was no more satisfied with his findings than Dr. Cope is. He felt that the appendix did not account for the picture. At the second operation the boy was operated on through an incision in the left upper quadrant, because of the x-ray findings. The splenic flexure was found to be virtually totally obstructed by a large, ragged, hard, infiltrating, obviously neoplastic mass, which was mostly on the medial side of the bowel, with some on the lateral and posterior aspects and ex-

tension down along the aorta and vena cava. It did not look like an intrinsic bowel tumor. At that time biopsy of two or three lymph nodes was done, but frozen section was inconclusive. The only thing that could be done was to relieve the obstruction; hence an enteroenterostomy around the lesion was performed, anastomosing the transverse colon to the sigmoid.

CLINICAL DIAGNOSIS

Intestinal obstruction.

DR. COPE'S DIAGNOSIS

Volvulus of large intestine?
Intussusception?

ANATOMICAL DIAGNOSIS

Colloid carcinoma of colon.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The biopsy showed a characteristic colloid carcinoma.

DR. LINTON: What was the grade of malignancy?

DR. CASTLEMAN: Colloid carcinoma of the bowel is extremely malignant. I think that it is commoner in children than is adenocarcinoma. I can recall one other case of colloid cancer in a child of seven or eight, who came in with a mass in the groin that proved to be a metastasis from a cancer of the sigmoid.

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NATIONAL RESEARCH COUNCIL ON FOOD RATIONING

Soon after the inauguration of a point system of food rationing in March, 1943, the director of the War Food Administration requested the National Research Council to appoint a committee of physicians to advise on special dietary needs and the best method of meeting them. This group was organized, with Dr. William D. Stroud, of Philadelphia, as chairman, within the Division of Medical Sciences of the council, as the Subcommittee on Medical Food Requirements under the general jurisdiction of the Committee on Drugs and Medical Supplies, of which Dr. Walter W. Palmer, of

New York City, is chairman. The recommendations of this committee have been published in the October 16 issue of the *Journal of the American Medical Association*.

Food rationing is recognized as a vexing problem, particularly so in a food-producing country such as ours, a country geographically immense, with extremes of climatic conditions, with dietary habits varying in different sections and among certain racial components, with geographical variations in food availability and distribution, and with many important food groups still unrationed. The recommendations of the subcommittee cover these qualifying factors, without attempting to "provide an exclusive compendium of conditions in which extra rations are thought medically indicated." It is further stated, "They [the recommendations] are rather a guide to the vast majority of such conditions, any attempt to define all of which would vitiate the scientifically necessary flexibility inherent in any wise system of rationing for the sick." Recognition has been made of the precedent established by the Food Rationing Advisory Committee of the British Medical Research Council, which acts in an advisory capacity to the Ministry of Food. In England, however, the problem is actually somewhat simpler owing to stricter rationing of a more limited supply of food, practically all of which is owned by a governmental agency of a geographically small and cohesive nation.

The recommendations of the subcommittee call for the restriction of the authority to certify patients to "persons licensed to practice medicine and surgery in their respective states," for appeal committees of qualified physicians, for the annual renewal of certification, and for certain maximal allowances in specified diseases, notably diabetes mellitus, tuberculosis, chronic nephritis of the nephrotic type, cirrhosis of the liver, severe hepatitis, chronic ulcerative colitis, chronic suppurative diseases and sprue. The diagnosis of chronic ulcerative colitis or of sprue is not accepted unless certified to by three physicians.

It is scarcely necessary to reiterate that food rationing constitutes a vexing problem. Processed foods present such a variety of types, from fruit juices that are mostly water to dried vegetables containing none, that it obviously makes little sense to measure them with the same yardstick or to weigh them in the same scales. The reason for grouping meats and fats is certainly one of organizational convenience that is not based on sound dietetic principles. Furthermore, a reasonably good sustaining diet can be built up of unrationed foods alone—when they are available.

In Massachusetts the policy of having a medical advisory committee to the state branch of the Office of Price Administration was adopted early in the summer, and this committee adopted the principle that, although it might be its brother's keeper, it did not wish to exercise police control over him. If a registered physician of Massachusetts wishes to employ dietary measures for the treatment of a patient and does so within reasonable limits and with apparently honest intent, the advisory committee will give him its support—nor does it challenge its colleagues' intellectual integrity by demanding the certification of three physicians for any diagnosis.

In our current years of trial, the more that can be accomplished by education and by mutual understanding and co-operation, the sweeter will be the taste of our ultimate success. It will be an unfortunate outcome if victory over our external enemies has to be won at the cost of increasing regimentation, coercion and force at home.

THE CHILDREN'S CENTER

THE Children's Center of Boston has now been in operation for over nine months, and the occasion seems suitable to review briefly its auspices, its purpose, its program and its accomplishments.

The Center was established in Roxbury, near a low-income community, in January, 1943, under the auspices of the Judge Baker Guidance Center

and aided by a grant from the Rockefeller Foundation. It was set up, however, as an independent organization, with its own staff under the direction of Dr. Marian C. Putnam and Mrs. Beata Rank. Its purpose was to provide day-nursery care and psychiatric consultation and treatment for infants and preschool children—a service that is almost unique, since the opportunity to begin educational and therapeutic guidance has hitherto rarely been offered in those family situations where emotional conflicts have appeared as early as the first or second year of the child's life. It is obvious that the best results can be obtained in these most formative years, and before unfavorable parent-child relations have become fixed.

The Center offers and has been furnishing a five-point program: day-nursery care, which is open to a group of thirty to thirty-five children with an age range from infancy to five years; inpatient care for a few children whose residence at home is temporarily inadvisable; therapeutic and educational work with parents and children; a consultation service available to the whole community; and facilities for the training and teaching of students in the various fields of child care. In this last respect, teaching programs are being offered for various professional people—social workers, nursery-school teachers, volunteers and students in child care and, ultimately, psychiatrists and pediatricians. A special grant from the Rockefeller Foundation helps to open the opportunity for study and research.

As evidence of the need that the Center is meeting and of the progress already made, it is interesting to note that during its first half year of existence applications were received for nearly 250 children. These came from thirty-seven agencies, from private physicians and through direct neighborhood contacts.

This new and valuable organization is particularly welcome in a community that, already richly endowed with them, knows how to utilize and appreciate its many health and social agencies.

MEDICAL EPONYM

HURLER'S SYNDROME

Although the term "gargoylism" as applied to this syndrome was first used by Ellis, Sheldon and Capon in an article entitled "Gargoylism (Chondro-Osteo Dystrophy, Corneal Opacities, Hepatosplenomegaly and Mental Deficiency)," which appeared in the *Quarterly Journal of Medicine* (29: 119-135, 1936), the source of the eponym is an article by Dr. Gertrud Hurler of the University Children's Clinic in Munich. Dr. Hurler wrote "Über einen Typ multipler Abartungen, vorwiegend am Skelettsystem [Multiple Degenerative Changes, Predominantly Skeletal]," which appeared in *Zeitschrift für Kinderheilkunde* (24: 220-234, 1919). A portion of the translation follows:

In the foreground of the clinical picture presented by our little patients stands the peculiar deformity of portions of the skeleton, namely of the head as a whole and especially the occipital region, of the clavicles, of the proximal end of the humerus and of the scapula. As the x-ray pictures show, we are dealing with changes in conformation particularly through extensive hyperostoses and defects (gaping sutures) in the skull, apparently the result of disturbances in ossification. The clavicles give the impression of being heavy, massive, excessively cured bony structures. The substance of the scapula seems very compact, the acromion markedly bulging, the joint socket shallow and small. In addition there is in both children a marked kyphosis, in one a funnel breast, in the other a pigeon breast, and in both, diffuse clouding of the cornea pronounced by the eye specialist to be hydropthalmia, that is, a congenital defect, and as further stigmas of degeneration there are in both children crooked little fingers and contractures of the fingers.

R W. B.

CORRESPONDENCE

BOOK REVIEWS

To the Editor In view of the recent critical review of the book, *Surgical Practice of the Lahey Clinic*, I would like to make two suggestions which, I believe, are constructive in character. These relate not only to this review but also to others to be published in the future.

This review is published anonymously, as has always been the custom of the *New England Journal of Medicine*, and my first suggestion is that all reviews be signed. This is but simple justice to the author and the publication, will make the reviewer more conscious of his responsibilities, and will permit readers to decide (1) whether the reviewer is a qualified critic and (2) whether his criticism might be colored by personal prejudice.

The second suggestion is less important. Since a review, to my mind, gives an opinion as to the value of a book, it should be presented to the reading public soon after publication. This review of *Surgical Practice of the Lahey Clinic* appeared two years after publication, and

after it had been, according to the W B Saunders Company, among the best selling books for the year of publication.

The book is composed, as is stated in the preface, of a group of selected papers previously published. These were written by a busy and often overworked staff of surgeons, fellows, anesthetists and other specialists in the Clinic, with a desire to share with other members of the medical profession the methods they had found useful. The authors would be the first to admit that the book is not what might be described as a literary gem. However, its enthusiastic reception, as evidenced by the large circulation and the many complimentary letters from purchasers, indicates that it has pleased many readers and apparently has answered a definite need.

As to the reviewer's comparison of the American and British literary style, it is probably true that the criticism so often leveled at us of being too utilitarian is also true of our literary style. However, we are Americans, and our literature is read largely by Americans. Today our American utilitarian methods are serving us and our respected English allies to an extent that is gratifying to them and to us.

As surgeons we are interested primarily in saving lives and limiting suffering. Secondly, we are interested in presenting our experiences to others to accept or to reject according to their judgment and trust in us.

FRANK H LAHEY, MD

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Boston

WAGNER-MURRAY-DINGELL BILL

To the Editor The time has come once again when it appears to me that one from the ranks should speak out frankly.

What I have in mind is the present approach in the way of argument in opposition to the Wagner-Murray-Dingell Bill, and similar proposals now before Congress.

It seems to me that any physician listening in on the "Forum of the Air" discussion of the evening of September 22, must have realized how much damage is done to the present methods of supplying medical care to the public by such forms of argument, either for or against the proposals. To my mind our leadership is weak in debate. The points presented are not persuasive. Brilliance of discussion is evident in full measure, but such points of view as are presented are antagonistic to the public. They gain us nothing in the way of support. On the contrary, they repel. Under such circumstances, one cannot fail to come out of the discussion with ignorance and prejudice, especially if there is profit in prejudice, without recognizing defeat.

The arguments of our leaders concern themselves with admitting gross defects. Our spokesmen seek sympathy and protection under the wings of our enemies. We pander to corporate practices of medicine, admitting that such practices are desirable. We strive to show that the bureaucratic groups are correct, and that we ourselves are attempting to do the very things that they propose. Therefore, we are now agreeing that they have been right all along, and that we have been wrong—that we are trying to do the same thing that they are trying to do,

and that we have been at fault. Such admissions are weak, nonconstructive and damaging.

Throughout recent years, when this problem has been acutely before us, I have adopted a very simple method of handling the situation insofar as the question has arisen amongst my personal contacts. I think that it has been practical, and I know that it has, in every case, been effective. Almost all the public are in favor of any method that will give them service at lower rates. They usually start off by telling me that they think it would be a wonderful thing. I agree with them, and add that it might work quite well for the medical profession. I point out that physicians have been donating services through clinics and hospitals to the extent of probably \$500,000,000 annually and that, in addition, poor collections in private practice virtually constitute a gift to the public of another enormous sum of indeterminate amount. I add that, if the Government or others took over the furnishing of medical care to the public, the doctors would be paid for all these present-day charity services. I tell them that, from a financial point of view, governmental supply of medical services might, and probably would, be a better thing for the doctors, since they would be compensated for these present charities by funds derived from taxation. I invariably find that the people who started off the conversation change their minds. They do not want anything like that if the doctors are going to profit or be paid by taxation or otherwise. They have come to think of doctors as public servants that should be poorly paid, or not paid at all. They tell me that they never thought of the matter from that angle. They are invariably converted, since they apparently are opposed to anything that will pay the doctors at any expense to themselves. Obviously, they were led to believe that they were going to get something for nothing.

Then on top of that I point out that many of the hospitals throughout the world have been provided through voluntary contributions by well-to-do citizens and that the Red Cross and other such organizations are likewise supported largely by voluntary contributions. I add that, if the Wagner-Murray-Dingell Bill or any similar bill went through Congress, these organizations would have to pass out of existence, insofar as control and voluntary contributions are concerned, and that they then would become a burden on the taxpayer.

I find that the public does not want state medicine under those terms, and it appears to me that some such general approach to the problem would be far more effective than the present one.

I do not believe that any businessman would argue his case in the way that our leaders are presenting their cringing arguments. He would approach the argument in a businesslike way. Looking for sympathy engenders only scorn. Admitting that we are wrong when we are not wrong, showing weakness when strength of argument should be our method, pandering, flattering and crawling, all seem to me to be the surest possible road to defeat. I believe that such methods have assured the passage of the Wagner-Murray-Dingell Bill during this session of Congress by an overwhelming majority.

Why not face facts squarely? I have no desire to sit here pounding out my heart and thoughts for publication in any wish for recognition as a leader. I desire no responsibility. But, it does stir up my wrath when I listen to such weak arguments, and see such bad leadership as

our spokesmen have given through these years in so many ways—leadership that is directing us straight into the path of defeat. Surely, some of us must have guts enough to come out squarely in such times, in order to try to let us see things straight and find a better way.

W. A. HUTTON, M.D.

Palmer, Mass.

REPORT OF MEETING

NEW ENGLAND PATHOLOGICAL SOCIETY

The first fall meeting of the New England Pathological Society was held in the auditorium of Boston University School of Medicine on October 21.

The first paper of the evening was "Immersion Foot and Allied Disorders" by Dr. Carl K. Friedland. Cooling the extremities of man to 15 to 18°C. causes simple vasoconstriction. Further cooling to, but not below, the freezing point results in tissue injury, an increase in capillary permeability and exudation of plasma into the tissues. Chilblain, pernio, trench foot and immersion hand and foot are all fundamentally due to the same pathophysiologic process, their apparent differences being the resultant of the site, type and duration of exposure. Other factors such as dependency, immobility, maintenance of body temperature and cold sensitivity also tend to modify the picture. Frostbite is designated as a separate entity because it is due to actual freezing and ice-crystal formation within the tissues.

In the discussion that followed Dr. Shields Warren described cases of prolonged immersion in which, after one and a half to two months, evidence of a mild to moderate Wallerian degeneration in the peripheral nerves was still present with an ultimate fair degree of recovery, although in one patient after six months a trophic ulcer due to anesthesia of the toe developed. In later periods there was pain thought to be due to fibrosis about the nerves. He also stressed the importance of the edema seen in this condition, which results in an increased amount of collagen with hyalinization so that the histologic picture simulates long-standing elephantiasis. The small arteries often show complete occlusion by old fibrous tissue, sometimes with recanalization consistent with the end result of thrombosis. Dr. Valy Menkin raised the point whether the substance responsible for the physiologic changes was due to histamine or a histamine-like substance. He believes that the changes are caused by a leukotaxin resulting in increased permeability, and cited experiments in which the exudate found in the tissues was dialyzed and the histamine-like substance and leukotaxin were removed. When this fluid was resynthesized with histamine, there was no change in capillary permeability. If the fluid was resynthesized with leukotaxin, the original effect was produced. He also raised the question of a neurogenic effect on the development of the inflammatory reaction. Dr. Moritz raised the question whether there were individual tissue specificities to thermal injuries, and in the discussion Dr. Warren brought out the point that the endothelium of the capillaries, small venules and lymphatics showed the earliest signs of injury, and he stated that he believed that this was the most susceptible tissue. Dr. Stanley E. Bradley presented the second paper,

Blast and Crush Injury During Warfare Extended naval operations and the bombing of crowded cities during the present war has aroused considerable interest in the immediate and remote clinical effects of the detonation of high explosives. Analysis of the physical character of an exploding charge indicates that the formation of a rapidly moving, high-compression wave front or blast may result in serious injury or death on land or in the sea unattended by marks of external violence. The syndromes of blast lung and water blast have been delineated and studied experimentally. In addition to the banal aspects of injury secondary to an explosion of any type, prolonged compression of the limbs by wreckage with subsequent renal damage and uremia has been seen fairly frequently and has inspired exhaustive experimental study. Renal functional changes during traumatic shock with special reference to the crush syndrome were briefly outlined.

In discussing the paper Dr Menkin raised the question whether there was elevation of glucose, the result of glucogenesis from injured tissue and whether the entire problem was related to the euglobulin fraction of the exudate—either euglobulin itself or a fraction, necrosed, causing particular injury to the liver and kidneys. The author's answer was that the carbohydrate metabolism was not altered there was variable but usually insignificant adrenal damage, with no evidence of liver damage. The question was raised whether a subdural hematoma could be produced by blast injury alone. In the discussion it was brought out that most cases of subdural hematoma were the direct result of trauma secondary to the blast pressure.

The last paper was presented by Dr Robert W Williams on the subject **Aviation and Cardiovascular System**. "In aviation the cardiovascular system must withstand two principal strains: centrifugal force due to sharp turns at high speed and low barometric pressure due to high altitudes. Centrifugal force in modern fighter planes may exceed eight times the force of gravity (8g). The vascular system in the dependent parts of the seated pilot is distended by blood under this tremendous force until there is insufficient blood circulating to the head. This causes visual blackout and then unconsciousness. The effects of centrifugal force may be counteracted by various mechanical devices that tend to prevent the pooling of blood in the lower parts of the body. At high altitudes the barometric pressure decreases until at about 50,000 feet it falls below the partial pressure of alveolar carbon dioxide and water vapor. Therefore at this altitude even with 100 per cent oxygen supplied by mask, life is impossible only with a pressurized cabin can man survive. Even at lower levels anoxia is proportional to altitude and causes not only central nervous but also cardiovascular pathophysiology. In addition, at altitudes above 18,000 feet, nitrogen dissolved in the tissues comes out of solution and may collect as bubbles. The symptoms of the bends—whether articular, pulmonary, cardiovascular or central nervous, depend on where these bubbles appear. The bends can be prevented by prebreathing oxygen, or better, by using pressurized cabins.

In discussing the paper the question was raised whether it is possible to train groups of aviators to tolerate these effects of centrifugalization. It was Dr Williams's opinion that this was not possible.

BOOK REVIEWS

Standard Nomenclature of Disease and Standard Nomenclature of Operations Edited by Edwin J Jordan, MD 12°, cloth, 1022 pp Chicago American Medical Association, 1942 \$4.00

This volume, *Standard Nomenclature of Disease*, first published as a book in 1933 revised in 1935 and now completely revised is combined with *Standard Nomenclature of Operations*, first published in June 1942.

The basic plan used for the work was adopted officially at the second National Conference on the Nomenclature of Disease. In 1937 periodic revision was taken over by the American Medical Association. In connection with the third edition a fourth National Conference on Medical Nomenclature was held under the auspices of the American Medical Association in Chicago in March, 1940 with Dr Haven Emerson of New York City serving as chairman. The present edition is the result of this conference. There is no essential change in the arrangement of the material in this edition, however, about thirty-five hundred additions, deletions and corrections have been made in individual diagnostic entries. The entries in the section Disorders of Endocrine Glands and Hormones which appeared in the classification

Body as a Whole in previous editions have been reclassified under the appropriate organs. The present edition is authoritative, since it represents the consensus of about sixty delegates to the conference from interested organizations and institutions.

Following the classification of disease, there is an extensive index referring to etiologic classification, and a useful table of eponymic diseases is appended. The aim of the work is to include every disease that is clinically recognizable and to avoid repetition and overlapping. English terms are employed, whenever possible, in preference to Latin or Greek terms although numerous exceptions occur, especially under diseases of the skin and of the eye.

The method of classification is based on two primary factors: the portion of the body concerned (topographic) and the cause of the disorders (etiologic). These two elements are designated by numerical digits separated from each other by a hyphen. The first three digits in the disease code describe the topographic site; the last three, following the hyphen, describe the etiologic agent.

The nomenclature of operations was compiled as a parallel to the code of disease in response to a demand from various sources. The compilation is a combination of all well known operative terminologies of various hospitals and associations. The division of fundamental surgical procedures into eight main categories was carried over, to a large extent from the *Classified Nomenclature of Operations* of the New York Hospital. This code attempts to bring about standardization in designating operations. It likewise has a complete index referring back to the various operations. All hospitals and others concerned with scientific medicine should adopt a standard nomenclature, particularly if they do not have a complete schedule of their own.

This book constitutes a standard reference source. It should be in the office of every surgeon and physician, especially those who are concerned with hospital service.

Borderlands of Psychiatry. By Stanley Cobb, M.D. 8°, cloth, 166 pp., with 28 illustrations. Cambridge: Harvard University Press, 1943. \$2.50.

Dr. Stanley Cobb, now psychiatrist-in-chief at the Massachusetts General Hospital, has long been a student of the borderlands of psychiatry. Beginning as a neuro-pathologist, with neurophysiologic leanings, he first became a neurologist, later an experimentalist and finally a psychiatrist. He has, during these years, wandered widely in the fields of the psychoneuroses, epilepsy, the organic disorders of the central nervous system, alcoholism and speech defects. This borderland, or to most psychiatrists the hinterland, contains, according to Cobb, a population of six million people, a vast number when compared with the six to seven hundred thousand who make up our hospital population for mental diseases, the primary field used for the major training center of most psychiatrists. With Cobb's background, therefore, physicians have long awaited the Lowell Lectures given by him in 1940. They will not be disappointed in this book, a somewhat elaborated and expanded text, geared to a more medical audience than usually attends a popular-lecture series.

Much of Cobb's training and fundamental thinking comes out in this book. He soundly views each field of the borderland, carefully evaluates the acreage, the quality of the soil, its previous history, its presumptive yield and its crop prospective in view of future tillage. Much of the field has been previously explored, such, for instance, as the old body-and-mind problem, now fertilized and revitalized as psychosomatics. Cobb presses and strains out the essentials in a brief, penetrating manner, leaving one sure of the way he feels, and almost certain that he is essentially right in his deductions. At least his review is based on a thorough study of each subject, neglecting no aspects, be they physiologic, anatomic, psychologic or psychiatric.

The whole book makes one think of a New England boiled dinner. There are many ingredients, all well cooked and furnishing sound, hearty fare. But one cannot digest quickly such varied provender as "the parallel evolution of speech, vision and intellect," "the function of the frontal areas of the human brain," "the anatomical basis of the emotions," "consciousness" and "concerning fits." Taken in small pieces, chewed and ruminated, each portion makes a tidy meal, and one well worth the time. Some psychoanalysts may not favor their portion, but neither will all the structuralists nor all the behaviorists. The meal, however, is excellent and everyone will find something at the table to his liking. If he does not, he had better go hungry.

The style of writing leaves something to be desired. Cases are treated "from more than one angle"; "cryptogenic" is discarded, as being a "long" Greek word, although Cobb does not hesitate to use "dysrhythmia," "anosognosia" or "strophosymbolia." Graves's name is constantly misspelled, as is that of Lorente de Nó and J. F. Fulton. There is a good index to the book, and selected references at the end of each chapter. The reviewer cannot conceive how anyone could not find both nourishing and thought-provoking sustenance in this stimulating, well-organized monograph. It is hoped that in future editions the textual errors will be erased.

Psychosomatic Medicine: The clinical application of psychopathology to general medical problems. By Edward Weiss, M.D., and O. Spurgeon English, M.D. 8°, cloth, 687 pp., with 2 tables, 9 illustrations and 4 charts. Philadelphia and London: W. B. Saunders Company, 1943. \$8.00.

The old body-and-mind relation takes on a fresh aspect when, in modern times, it becomes "psychosomatic medicine." A periodical, first issued in January, 1939, with the designation *Psychosomatic Medicine*, was the early effort in the field. Now comes a book, stemming from the same impulse. The senior author learned about twenty years ago that one patient's illness, the chief symptom being headache, "was her infantile way of expressing disapproval of her brother's marriage and, when the meaning of the illness was made clear to her, she promptly recovered." Now he finds that similar cases are by no means the exception in the practice of medicine. Many authorities, he states, agree that cases like the above constitute about a third of all practice, and that another third concern patients who have emotional factors complicating and adding to the burden of their physical disease.

This book deals with the problems of the emotional factors in the cause or augmentation of illness. The volume stresses personality development and the establishment of psychopathology early in life. In a series of chapters, each division of the body structure is taken up in detail. The gastrointestinal and cardiovascular systems, as might be expected, receive most attention, but the endocrine, special-sense and the genitourinary systems are not neglected. There is a brief chapter on military medicine, a timely effort but somewhat out of place in this volume, and four final chapters on treatment.

In the opinion of the reviewer, the book presents a mass of data, somewhat poorly evaluated and often presented without ordinary scientific discrimination. Many case histories are used, but they are often feeble arguments for positive generalizations. As in the case noted above, all symptoms tend to disappear only too quickly once the inner springs of discord are touched. In other words, the authors make happy endings almost as frequent as in motion pictures, a goal seldom reached in the practice of most psychiatrists.

In spite of these shortcomings, the book offers much thoughtful material for medical students and practitioners. It at least brings forcibly to their attention one of the most pressing problems in medicine today. The authors demonstrate that the emotions may play a role in illness, as in our daily lives; what they fail to show in an entirely convincing manner — possibly the time is not ready to show it — is how that role is played. From time immemorial emotions have colored our lives; this book leads one to believe that the coloring early in life is of greater importance in disease than any coloring that may come later and that many illnesses, the result of pathologic changes, come as the result of the emotional strain. Although there is some evidence that such statements may be true, much more must be known before a broad generalization can be made. This book forms part of the stimulus that arises from an awakened interest in psychosomatics and, as such, deserves a wide reading.

(Notices on page xii)

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ENDOCRINE AND PSEUDOENDOCRINE PROBLEMS IN CHILDHOOD*

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BOSTON

RIGHTFULLY endocrine and pseudoendocrine problems in childhood deserve consideration together. Many anomalies and disturbances of growth and development and certain cases of retarded sexual development, of an abnormal accumulation and distribution of fat, of dwarfism and even of mental retardation are often mistakenly grouped as the expression of an endocrine imbalance. There are many more, and to a certain extent more important, problems that are often considered as endocrinopathies but that have only a very loose relation, or no relation at all, to a disturbance of one of the hormone glands. Regarding true endocrinopathies that are of importance in general pediatric practice, if one were to count them on the fingers of both hands, there would certainly be quite a few fingers left over.

There are three large groups of diseases and anomalies that have certain features in common but that differ from each other by their etiology as well as by the dominance of certain characteristics. These characteristics determine the condition in question and classify it under the heading of one of these three groups, which are as follows:

Group 1. True endocrine disorders caused by a pathologic process or anomaly of an endocrine gland, which may be even a congenital absence.

Group 2. Accentuations of physiologic phases of development, which sometimes imitate true endocrinopathies. Constitutional and familial factors are frequently involved. Transitory states, such as transitory infantilism, certain forms of obesity and disharmonic development, should be included.

Group 3. Congenital anomalies and multiple deviations, retardation of development, somatic

as well as mental, sometimes mistaken for endocrinopathies and showing some of their essential features. Nor infrequently they overlap. This group should properly be called genopathies rather than endocrinopathies.

When dealing with a possible endocrine disorder in childhood, certain routine measures should be carried out so that the condition may be more accurately classified. The following is a brief outline of such a scheme:

Exact body measurements (standing and sitting height, circumferences of head and chest, breadths of chest and pelvis, and span); appraisal of proportions (stem index); velocity of growth and relative growth rate when the patient is observed over a longer period of time.

Determination of the bone age by x-ray; eventually, x-ray examination of teeth and skull.

Appraisal of the genital and extragenital characteristics.

Examination of eyegrounds and visual fields.

Laboratory tests appropriate to the given case, such as basal metabolic rate, specific dynamic action, sugar-tolerance test (glucose or galactose), determination of blood cholesterol and cholesterol ester levels, and assays of sex hormones in the urine and follicle-stimulating hormone in the blood. (Certain laboratory tests are important only for selected cases, such as the insulin-tolerance test and the dextrose-insulin tolerance test in the diagnosis of endocrinologic disorders of dextrose metabolism, and determination of the sodium and potassium levels in cases of possible suprarenal involvement.)

Psychometric tests.

Accurate records of response to treatment.

In the physical examination, special attention should be given to hematologic studies (hypochromic anemia in myxedema), the heart and electrocardiogram (characteristic changes in hyperthyroidism and hypothyroidism), the blood pressure (elevation in adrenocortical obesity with macrogenitosomia) and the size of the liver (hep-

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 26, 1943.

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atomegaly in dwarfism due to glycogenesis). All cases should be examined from the point of view of somatic stigmas, according to a certain schedule, which space does not permit discussing in detail here. Of particular interest is the mesenchymatous group of stigmas, such as curved fifth finger, brachydactylia, fusion and other anomalies of the ribs, malocclusion, ear nodules and so forth—not only their presence but also their occurrence together.

To illustrate Group 1, the true endocrinopathies, I shall select only two examples—congenital cretinism and pituitary dwarfism.

Figure 1 shows a case of congenital cretinism in a child of five weeks with all the characteristic signs. Early diagnosis and treatment are essential

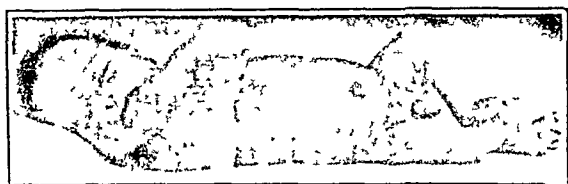


FIGURE 1. *Congenital Cretinism in a Five Week-Old Baby (Nobel et al.¹).*

The photograph shows the characteristic facies, the macroglossia and an umbilical hernia

in order to prevent further progressive stages of deterioration, which are never completely reparable, as is demonstrated in Figure 2. Even if the somatic development shows good progress, as illustrated by the improvement of skeletal development under the influence of thyroid treatment, the end result is poor so far as mental development is concerned.

The next example is concerned with pituitary dwarfism. Many mistakes are still made in the diagnosis, although it is usually quite simple. Figure 3 shows a pituitary dwarf of fourteen years. The only obligatory clinical signs are dwarfism and complete failure of sexual development if the condition has an onset during the early period of childhood, or atrophy of the genitalia if these have developed before the onset of the condition. The lack of mental retardation is important. All the other signs and symptoms, such as obesity, gero-derma and diabetes insipidus, and many of the laboratory findings are nonobligatory for the diagnosis. Changes of the eyegrounds and visual fields may or may not be present, depending on the site of the lesion and the duration of the process. The underlying lesion in the case shown in Figure 3 was a cystic tumor of the hypophyseal duct, consisting of squamous epithelium. The same picture may be observed without the presence of a tumor. The primary deficiency in pituitary dwarf-

ism may be the result of congenital absence of the acidophilic cells, surgical ablation, pressure necrosis, infection, infarction, calcification or any destructive lesion in or in the immediate vicinity of the gland. The midbrain is sometimes involved,



FIGURE 2. *Congenital Cretinism in a Seventeen-Year Old Girl (Nobel et al.¹).*

Before treatment (photographs on left), the height and bone age corresponded to those of a child of one and a half years. After seventeen months of thyroid treatment (photographs on right), the height had increased 18 cm. and there was striking progress in skeletal development.

with repcussion on the gland. One of the youngest cases on record is now under observation at the Boston Floating Hospital and the Boston Dispensary (Fig. 4).

The treatment of pituitary dwarfism consists of surgical removal of an existing tumor and of hormone therapy in the other cases. Methyltestosterone, which is given by mouth, is the best of the preparations available at this time for the hormone treatment of pituitary dwarfism (Fig. 5). It is a specific factor stimulating linear growth and the interstitial tissue of the gonads. The drug stimulates the development of the secondary sexual characteristics but has no influence on the maturing process of the gonads proper. It does not stimulate spermatogenesis and therefore does not lead to early closure of the epiphyses. Only completed sexual maturity arrests skeletal growth and leads to the fusion of the epiphyses. The growth-

stimulating effect of testosterone derivatives in hypogonadal subjects has been studied by several investigators (Moricard and Bize,⁴ Villaret, Justin-Besançon and Rubens-Duval,⁵ Webster,⁶ Webster and Hoskins,⁷ and Browne and Ross⁸). The in-

and those giving negative follicle-stimulating hormone tests with the urine. The cases in the latter group exhibit a rise in the 17-ketosteroid assay with chorionic gonadotropin therapy. Albright and his co-workers believe that this syndrome is of pi-

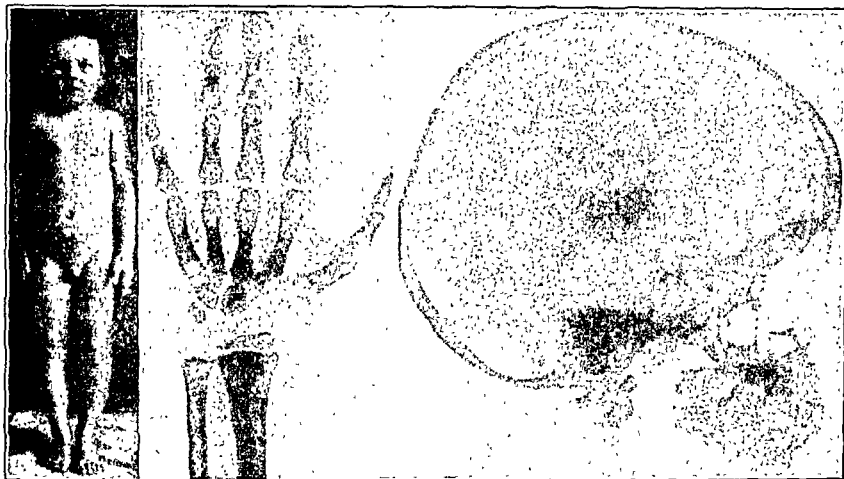


FIGURE 3. Pituitary Dwarfism in a Fourteen-Year-Old Boy (Nobel et al.¹).

The height was only 107 cm., corresponding to that of a child of five and a half years. The bone age was consistent with that of a child of three years. The testicles were atrophied, and there was atrophy of the optic nerve, with temporal hemianopia. The x-ray film of the skull shows a suprasellar cyst and increased convoluted markings.

roduction of a methyl radical greatly enhanced the peroral effects of testosterone, as shown by Miescher and Tschopp.⁹

Pituitary hormones and the chorionic gonadotropins are on the whole a disappointment so far as the treatment of pituitary dwarfism is concerned. So long as there are no synthetic hormones available, as, for example, in the case of the sex hormones, but only crude extracts, the therapeutic results are doubtful and not consistent. On the other hand, in some supposedly hypopituitary conditions—for example, in certain selected cases of cryptorchidism—treatment with chorionic gonadotropins is valuable.

In the differential diagnosis between panhypopituitarism and male eunuchoidism the 17-ketosteroid assay and that of the follicle-stimulating hormone test in the urine have recently become of great importance. According to Fraser, Forbes, Albright, Sulkowitch and Reifstein,¹⁰ patients with panhypopituitarism have no 17-ketosteroids or very low assays. Cases of male eunuchoidism are divided into two groups, those giving positive

pituitary origin. Chorionic gonadotropin produces no rise in the 17-ketosteroid excretion in male castrates and in eunuchoid patients with positive follicle-stimulating hormone tests.

Group 2, the pseudoendocrinopathies, is composed of those children who at some time during their growth period deviate from the normal but who do not have a real abnormality of any of the endocrine glands. A great number of prepubescents, who will ultimately develop into normal adults, are often mistakenly diagnosed as having endocrine disturbances. The problem in these cases relates to the size of the genitalia, obesity or growth. One of the commonest errors is concerned with the management of obese boys. The distribution of fat in these boys resembles that found in women and adult eunuchs. The physician is therefore inclined to make a diagnosis of obesity of the Fröhlich type, particularly since the genitalia appear small. This type of obesity is not at all abnormal in boys of a pyknic somatotype. The apparent hypopituitarism is due to the fact that the penis is usually embedded in suprapubic fat. When the fat pad

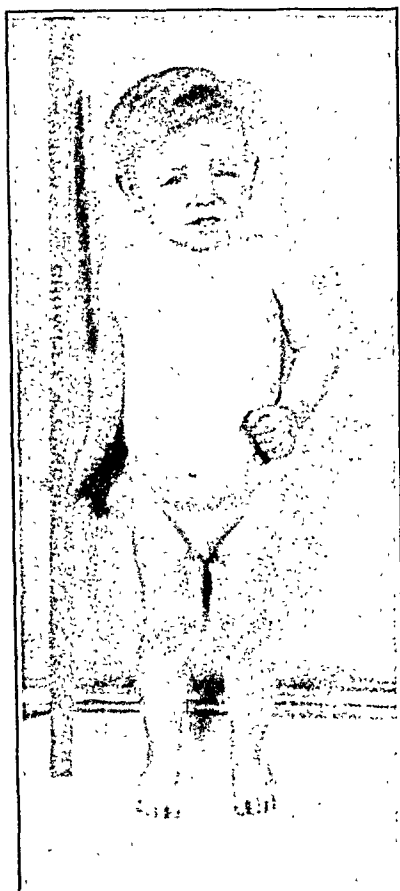


FIGURE 4. Pituitary Dwarfism in a Three-and-a-Half-Year-Old Boy.

The height was only 75 cm., corresponding to that of a child of one year, as did the bone age.

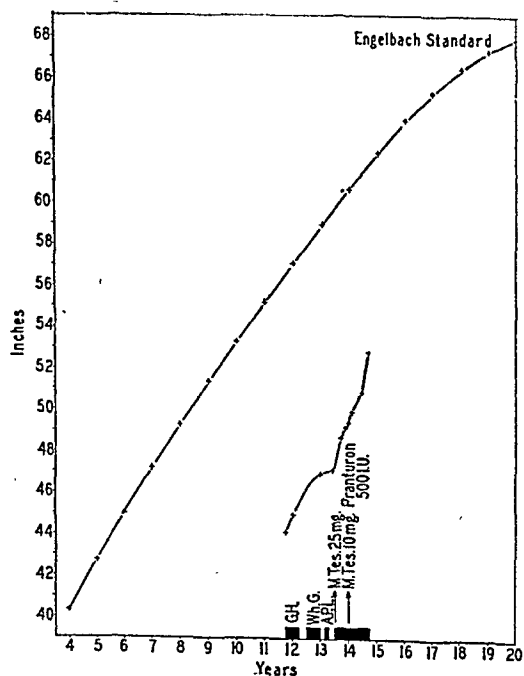


FIGURE 5. Stimulation of Growth in a Pituitary Dwarf.

The growth curve is compared with Engelbach's standard. The abbreviations are as follows: G.H., growth hormone; Wh.G., whole gland; A.P.L., anterior-pituitary-like hormone; and M.Tes., methyltestosterone.

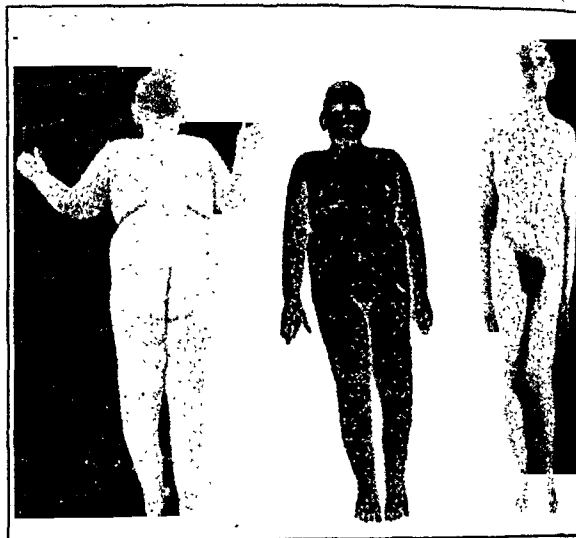


FIGURE 6. Pseudo-Fröhlich Syndrome in a Fourteen-Year-Old Boy (Rosenstern²).

The boy was of normal height but was markedly obese, with the testes embedded in suprapubic fat. The condition subsided spontaneously, and at eighteen years of age (photograph on right) the boy had normal build and complete sexual development.

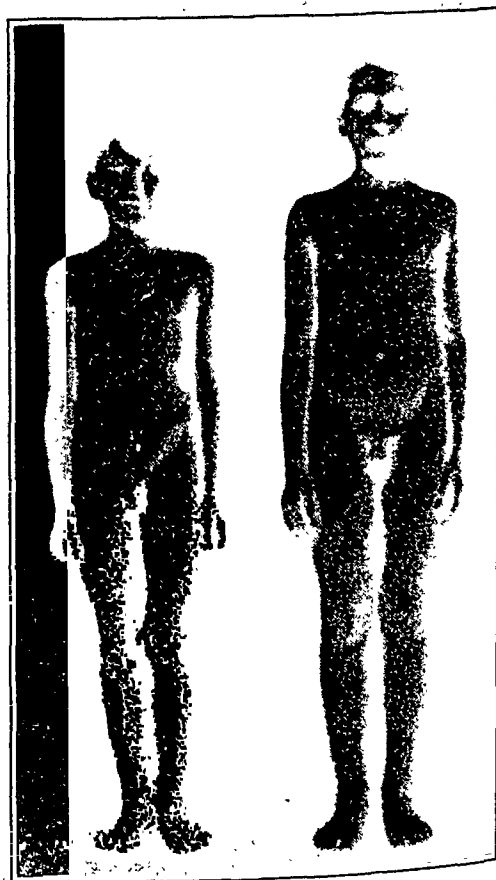


FIGURE 7. Temporary Early Leanness (Rosenstern²).

The photograph on the left shows leanness at eleven years of age; that on the right, an appreciable fat deposit with the advent of puberty at thirteen.

is pushed back and the penis and testes are measured, the genitalia are found to be within the normal range, furthermore, there is no delay in the onset of pubescence and development may occur earlier than usual. Since there is no hypogonadism, the diagnosis of adiposogenital dystrophy of Frohlich's type is not at all justifiable. After reaching the age of maturity, most of these boys grow taller and slimmer, although they maintain their characteristic somatotype through life. Treat

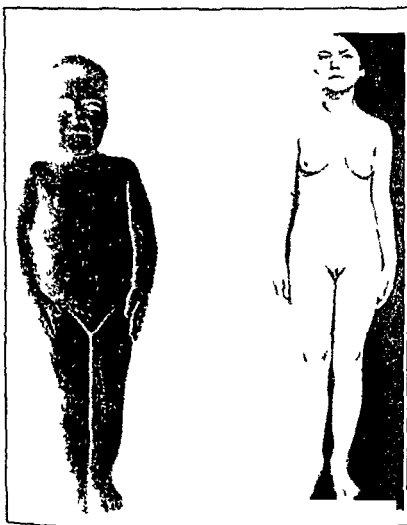


FIGURE 8 *Temporary Early Obesity (Rosenstern*)*

The photograph on the left shows obesity at five and a half years of age; that on the right the normal build acquired spontaneously at thirteen.

ment consists of a low caloric diet, particularly low in carbohydrates and fat, supported by thyroid medication (Schonfeld¹¹). At the beginning it is advisable to adjust the intake below the basal metabolism and induce the patient to burn his own body fat.

Figure 6 shows a case of pseudo Frohlich syndrome. At fourteen years the patient had all the characteristics of obesity of prepubescence. Four years later all signs had subsided. He is now completely mature. No specific treatment was supplied. The pseudo Frohlich syndrome occurs in girls as well as in boys. There are other pseudo endocrine problems in girls, some of which are concerned with anomalies of the menstrual period.

That in many of these cases of obesity one is dealing simply with an accentuation of a physio

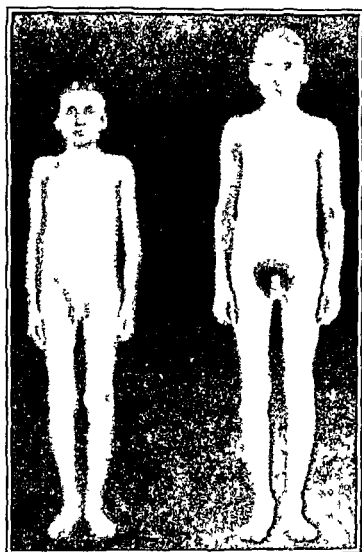


FIGURE 9 *Late Sexual Development in Universal Infantilism (Rosenstern*)*

The photograph on the left shows that sexual development had not begun at the age of seventeen; that on the right, that it had been completed at twenty-two. The patient suffered from chronic asthma.

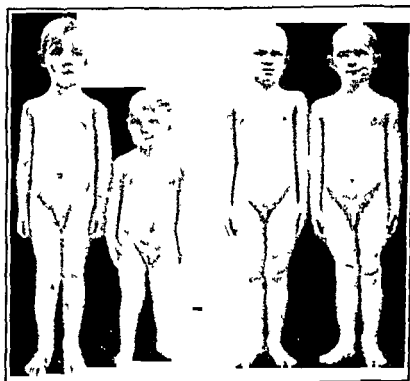


FIGURE 10 *Temporary Stunting of Stature (Rosenstern*)*

In the photograph on the left, the boy on the right is much shorter than the normal boy of five and a half years; on the right, in that on the right the same boy (at the right) is equal in height to a normal boy of seven and a half years (at the left).

adjuncts to the plication technics in increasing the number of favorable results. The best promise of satisfactory treatment, however, has issued from the recent work of Kennedy.

Most plastic operations involving the vesical neck and urethra are based on the original Kelly⁴ principle, which outlines the mattress suturing of the bladder neck and urethral sphincter. Briefly, the operation consists of exposing and separating the urethra and bladder through a longitudinal incision in the anterior vaginal wall and the approximation of the torn or relaxed sphincter muscles and fascia.

Kennedy⁵ describes the most frequent causes of incontinence as follows: trauma to the inner and middle third sphincters of the urethra, causing them to become partially fixed by fine bands to the posterior lateral margins of the adjacent pubic rami; and damage in the midline to those voluntary fibers that pass under the middle third of the urethra and are attached to each ramus of the pubis, posteriorly constituting a sling support.

Subsequent to a careful study of the anatomy and physiology of the bladder and urethra, and after the use of roentgenography in elaborating the function of the urethra, Kennedy reported that it was possible to cure incontinence by breaking down the fine bands between the urethra and the pubic rami and plicating the urethra in its midline to prevent any further connection with the rami laterally, and bringing together in the midline beneath the inner and middle thirds of the urethra the injured "sling" fibers. He⁶ reasoned that the voluntary sphincters functioned better when they were circular and without attachments and were suspended freely in a sling. He presented a detailed exposition of the technic employed to obtain these conditions.

The reports of the results in operative procedures for urinary incontinence vary according to the methods used and the ability of the plastic surgeon, as well as the period of time that elapses between the injury and its repair. It is obvious that the fascia and muscle fibers to which Kennedy attaches so much importance are available for only a limited time. Their attenuation after years of relaxation and injury makes their approximation problematical and the end results irregular. Since many of the women who seek treatment have endured incontinence for years, the reports of satisfactory repair show remarkable variation. One of the early papers concerning the surgical treatment of urinary incontinence is that of Kelly and Dumm,⁷ who had successful results in 75 per cent of 20 treated cases. Watson⁸ operated on 105 cases, with success in 66 per cent, improvement in 22 per cent and no improvement in 12 per cent.

He also found that two out of three patients with incontinence showed a cystocele.

Furniss^{9, 10} reported 17 cases of incontinence treated surgically. Success was obtained in 76 per cent and relief of symptoms in 11 per cent, and there was operative failure in 13 per cent. Of 28 consecutive operations by Kennedy,⁶ only 2 were failures; that is, 93 per cent were completely satisfactory. Peightal,¹¹ in a discussion of Kennedy's work, revealed that 11 of 12 cases were successfully treated by the latter's technic. Stress incontinence was present in the single failure. According to Barnes,¹² the cures vary from 36 to 100 per cent and repeat surgery from 6 to 15 per cent. He emphasized the general inadequacy of the treatment. Matassarini¹³ revealed that 10 to 20 per cent of the patients visiting Schaumann's gynecologic clinic have urinary dribbling and 1 to 2 per cent have complete loss of control. He believed that 90 per cent of these patients would secure continence from simple cystocele repair and that the remaining 10 per cent would respond only to a more extensive operative procedure. In his hands, plication of the urethra in the anteroposterior plane with the addition of Kelly stitches placed at the trigone resulted in a complete cure in 6 cases. Berkow¹⁴ stated that when the Kelly technic is employed, 15 to 40 per cent failures are revealed by the literature. His own procedure differs from that of Kennedy in that he does not free the fascial sling so widely, but rather raises the urethra to the clitoris and closes the structures beneath it. He analyzed 19 cases from two months to three years after operation and found that 89 per cent were continent. Aldridge³ believes that 10 to 20 per cent of the operations for urinary incontinence fail.

TECHNIC OF KENNEDY OPERATION

In the Kennedy operation for incontinence, the cervix is fixed by a Jacob's volsellum, if it comes down readily; if not, the anterior vaginal wall is picked up at the level of the uterine isthmus by a guy suture of black silk. A second guy suture of the same material is placed in the anterior vaginal wall 1 cm. below the urinary meatus. A longitudinal incision is made in the anterior vaginal wall between these two sutures. It starts about 1.5 cm. below the urinary meatus and ends about 1.5 cm. above the suture placed at the level of the uterine isthmus. The anterior vaginal wall is dissected from the urethra and the bladder (Fig. 1). The urethra is next separated from the pubic ramus on each side. By starting the separation close to the bone, a plexus of veins and branches of the inferior vesical artery may be avoided. If these vessels are torn, they are picked up and ligated with fine chromic catgut.

The separation is carried out into the paravesical space. This dissection is facilitated by retracting the edges of the vaginal wall by means of guy sutures of black silk or by Allis forceps. The

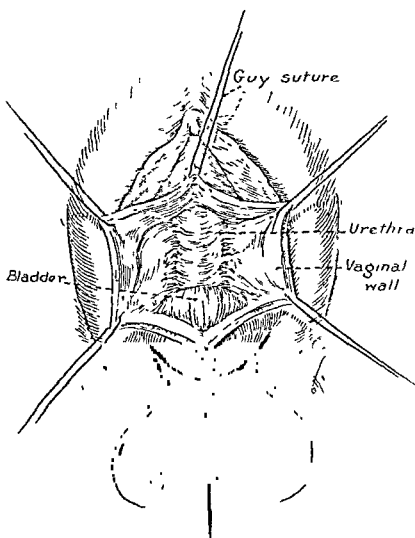


FIGURE 1.

The anterior vaginal wall has been opened to within 1.5 cm. of the external urinary meatus. The urethra has been separated from pubic rami, and the bladder neck is exposed.

fibrous adhesions between the urethra and the pubic rami having been severed, the former regains its mobility. In order to restore and maintain continence, the urethra must not be permitted again to become adherent to the pubic rami. With this end in view, the tissues under the urethra are plicated by three mattress sutures of No. 1 chromic catgut, which, when tied, keep the urethra away from the pubic rami (Fig. 2). A second row of three mattress sutures introduced in the edges of the fascia-like structures on each side of the urethra further separates it from the pubic rami (Fig. 3). If necessary, a fourth mattress suture may be placed at the lower part of the urethra in the region of the internal sphincter (a suture placed in this region formed the basis of the Kelly operation for incontinence). The excess of the anterior vaginal wall on each side that formed the urethrocele is then resected. In accomplishing this, the damaged portion of the voluntary sphincter is removed with the vaginal wall.

The intact voluntary sphincter fibers that remain after the resection of the vaginal wall are approximated by No. 1 chromic catgut-sutures, usually three in number, with simultaneous closure of this portion of the anterior vaginal wall. These chromic catgut sutures begin at the highest point of the vestibule and extend down about 2 cm. In their course, they pick up the vaginal wall close to the pubic rami, so as to enclose the muscle fibers of the constrictor urethrae muscle (voluntary) and the inferior layer of fascia of the uro-

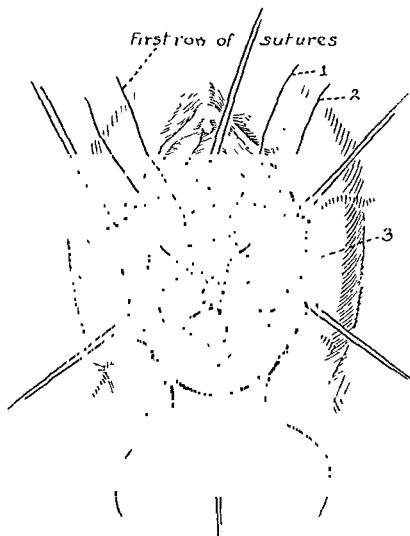


FIGURE 2.

Three mattress sutures of No. 1 chromic catgut have been placed in the fascial structures on the sides of the urethra. When tied, they pull the urethra away from the pubic ramus of each side. The lower mattress suture (3) plicates the vesical sphincter.

genital diaphragm on both sides. The remainder of the anterior vaginal wall is closed with similar sutures (Fig. 4). Originally, we used silver wire for the three uppermost sutures in the anterior vaginal wall, as recommended by Kennedy, but this has been replaced by No. 1 chromic catgut sutures without any apparent change in the result. A plain, male soft-rubber catheter is introduced into the urethra and left in as an indwelling catheter for seven days. The patient usually voids normally after its removal, and she is allowed out

of bed on the tenth postoperative day. Figure 5 illustrates the completed operation.

RESULTS

A detailed survey of 23 cases, all of which received typical Kennedy operations, revealed the following data. The average age of patients was 47.1 years, the youngest being thirty-five and the oldest sixty-nine. In the thirty-to-thirty-nine-year group there were 4 cases, in the forty-to-forty-nine year group 13 cases, in the fifty-to-fifty-nine-year group 2 cases, and in the sixty-to-sixty-nine-year group 4 cases. The average parity was 3.6. Primigravidas numbered 3 (13 per cent), biparas 3, triparas 5 (22 per cent), quartiparas 5, quinparas 4 (17 per cent), sexiparas 2 (9 per cent) and septip-

aras 1 (4 per cent). Seven (30 per cent) of the patients had undergone previous operations for their urinary incontinence; in 5 of these cases (22 per cent) the procedures were cystocele repairs.

The presenting symptom of incontinence had existed for widely divergent lengths of time, with an average period of ten years and three months. The shortest duration was seven months and the longest thirty-two years. Three patients (13 per cent) had had incontinence for less than one year, 4 (17 per cent) for one to four years, 6 (26 per cent) for five to nine years, 6 for ten to nineteen years, 1 (4 per cent) for twenty to twenty-nine years, and 1

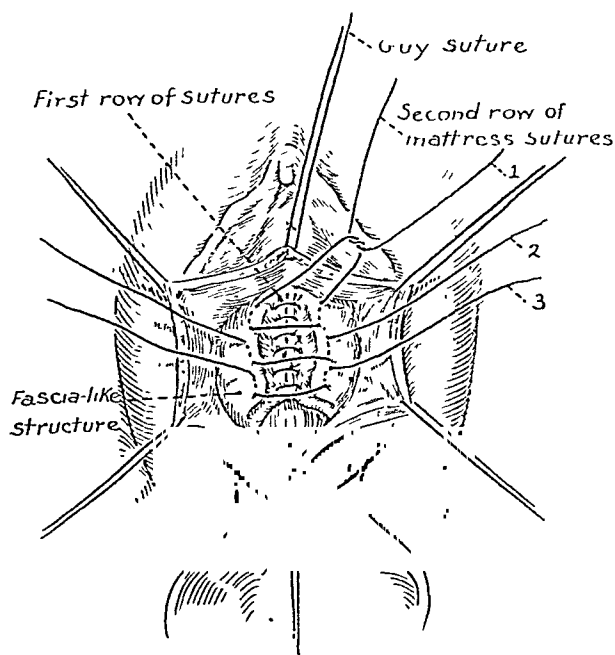


FIGURE 3.

A second row of three mattress sutures of No. 1 chromic catgut has been placed in the fascia-like structures on the sides to enfold further the urethra and pull it away from the pubic rami.

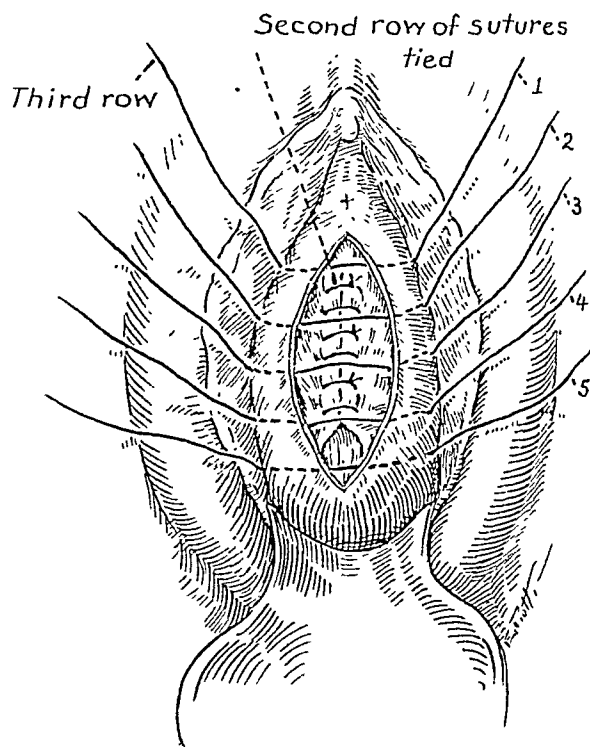


FIGURE 4.

The constrictor urethral muscle and the urogenital diaphragm have been reconstructed, and the remainder of the incision in the anterior vaginal wall is about to be closed.

cystocele, 10 cases (44 per cent) of relaxed vesical sphincter, some with previous cystocele repair, and but 3 cases (13 per cent) of relaxed urethral sphincters alone. Seventeen of the patients also received gynecologic surgery in addition to the Kennedy operation; namely, trachelorrhaphy in 1 case, the Manchester operation in 3 cases, posterior colporrhaphy in 2 cases, perineorrhaphy in 12 cases, hysterectomy in 2 cases, and cervical amputation in 5 cases. Only two anesthetics were used — spinal in 14 cases (61 per cent) and general in 9 cases (39 per cent). The average length of hospitalization was 17.1 days, with the majority of patients (18 cases) remaining for thirteen to sixteen days. Except for mild transient cystitis (5 cases) that responded immediately to conservative therapy, there were no postoperative complications.

All the patients were successful in controlling their urine two to four weeks postoperatively. One woman who had a dilatation and curettage.

cervical amputation, Kennedy operation and perineorrhaphy experienced some hesitancy at the beginning of micturition, but this gradually disappeared. The late results were likewise gratify-

ing. was excellent, but within 2½ years the stress incontinence had returned to its original degree. In retrospect, this case might have responded better to such a procedure as that of Aldridge,³ in which abdominal fascia is used as a sling for the weakened urethral sphincter.

CASE 2. Mrs. H. C., a 41-year-old tripara, had had incontinence for 7 years associated with a relaxed sphincter. Throughout her 14 days in the hospital, the bladder function was perfect, but 3 months later the incontinence was as severe as on entry.

DISCUSSION

The need of a careful urologic study in incontinent women is self evident. Barnes¹² has suggested three tests for adequate diagnosis and evaluation of the type of incontinence, giving the technic of each: direct measurement of intravesical pressure, direct measurement of urethral resistance and indirect measurement of internal sphincter strength. His work emphasizes the fact that stress incontinence is the result of failure of the voluntary urethral sphincter fibers to function. The involuntary fibers control other vesical pressures. This suggests that operations such as that of Aldridge³ are of great benefit in cases where stress incontinence is superimposed on general urinary dribbling. The inadequacy of the Kennedy procedure alone in such cases is well illustrated in the first of our two failures.

It is important to re-emphasize the significance of the lapse of time between the injury that caused the incontinence and the treatment of the condition. In our first failure seventeen years had elapsed, and in the second seven years. It is possible that an incontinent patient with a cystocele and urethral sphincter relaxation of more than five years' duration requires more than an anterior colporrhaphy. In especially recalcitrant problems resort to the methods of Goebell² and Aldridge³ is of real value.

SUMMARY

A presentation of the general problems of urinary incontinence in women is made.

Twenty-three women with incontinence were treated by the Kennedy operation, with either marked improvement or complete late recovery of bladder function in 91 per cent in an average of seventeen months after operation.

Two failures occurred in the series; the possible causes for failure are discussed.

Suggestions are offered regarding the study, classification and treatment of urinary incontinence in women.

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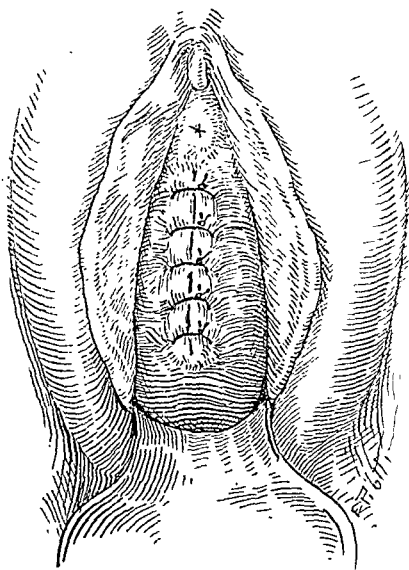


FIGURE 5.

This sketch shows the result of the completion of the operation.

ing. Late check-ups on all the patients included in this report were obtained from two months to four years and nine months after operation, with an average period of seventeen months. Complete late recovery of bladder function was attained in 18 cases (78 per cent), and marked improvement in 3 cases (13 per cent). The total number of cases with either complete recovery or marked improvement was therefore 21 (91 per cent). The failures numbered 2 (9 per cent); a study of these follows. In no case was there any aggravation of symptoms after surgery.

CASE REPORTS

CASE 1. Mrs. M. H., a 46-year-old quartipara, had had dribbling and stress incontinence for 17 years. A relaxed vesical sphincter and moderate cystocele were present. No previous surgery had been attempted. A dilatation and curettage, Kennedy operation and perineorrhaphy were done under spinal anesthesia, and the postoperative convalescence was uneventful. When a discharge examination was made 15 days after surgery, the urinary control

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CLINICAL NOTE

ACTINOMYCOSIS OF THE CHEST WITH SPREAD TO THE ABDOMEN*

REPORT OF A CASE CURED WITH SULFADIAZINE

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BECAUSE of the known severity of actinomycosis, particularly with thoracic involvement, we have thought it worth while to present the following case. The older literature shows a poor prognosis for actinomycosis of the chest. Of the cases reviewed at the Royal Victoria Hospital by Morton,¹ 5 out of 7 thoracic cases resulted in death. This was in contrast to the somewhat better prognosis for the abdominal cases and the considerably better prognosis for the cervicofacial group. This impression is confirmed by Cope,² Hanes³ and Schmitt and Olsen.⁴

In the last five years a number of reports of successful treatment of actinomycosis with sulfonamides have appeared. The first is that of Walker,⁵ who treated a soldier with appendiceal actinomycosis and a draining sinus. Sulfanilamide was used, with dramatic results. Following this case, the reports of Hall,⁶ Sudler and Johnson⁷ and Miller and Fell⁸ in this country and of Dorling and Eckhoff⁹ and Ogilvie¹⁰ in England appeared in fairly quick succession. Others¹¹⁻¹⁴ followed. The cases reported were all treated with sulfanilamide or sulfapyridine, with cure or improvement. In some cases other means of treatment, such as x-ray and iodides, were used together with the sulfonamide drug. The use of sulfathiazole is reported in only 1 case, in which it was unsuccessful after a very short course of therapy.¹⁵ Two of the cases reported above were of the thoracic type

(Wilkinson¹¹ and Dobson et al.¹³). None of these reports contain cases treated with sulfadiazine.

The rationale of the sulfonamide treatment of actinomycosis has been studied by Cutting and Gebhardt,¹⁶ who have shown that the growth of *Actinomyces hominis* in vitro is inhibited by the drugs. Of the drugs studied by these authors, sulfathiazole and sulfadiazine were found to be about equally effective and to be more effective than sulfanilamide in similar concentration. On the strength of this study and because of the low toxicity of sulfadiazine, it was used in the treatment of our case.

CASE REPORT

D. O'K., a 9-year-old boy, was admitted to the Surgical Service of the Children's Hospital on January 31, 1942, complaining of draining sinuses of the back and right flank.

Sixteen months before admission the patient had developed a cough and fever. This continued until 14 months before admission, when an egg-shaped swelling appeared on the right chest posteriorly. The patient's physician sent him to a hospital near his home, where it was thought that he had empyema necessitatis. An x-ray film of the chest showed slight density at the right base, which was interpreted as probably in the lung rather than in the pleura. This swelling was drained and proved to be an abscess. Surgical and medical measures were undertaken, and during the next 12 months the patient underwent six operations for drainage of persistent and spreading abscesses on the posterior chest and in the right flank. The right pleural and subdiaphragmatic spaces were opened for drainage during this time. He is reported to have been given sulfapyridine and sulfanilamide at times, but the quantity given and the duration of treatment were unknown. Clinically he did poorly, with profuse drainage and gradual loss of strength. Two months before admission he was taken home from the local hospital against the advice of his physician.

During his stay at home the patient continued to go downhill. He was feverish in the evening and coughed continuously. On two occasions he coughed up blood. Also, he developed pain on straightening his right leg. His condition grew progressively worse, and he was admitted as an emergency case 16 months after his first symptoms.

The patient lived in the factory district of a small New England shoe town. His mother and father and one brother were healthy. The past history was negative.

Physical examination showed a feverish, emaciated and apprehensive boy weighing only 49 pounds. He was

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occasionally seized with paroxysms of coughing. The skin was loose, pale and dry, and was covered with fine lanugo-like hair. The back was honeycombed with sinuses interspersed with raw areas of granulation. Thick, yellow pus could be expressed from the sinuses. One sinus extended into the right flank, apparently beneath the liver, for the length of a Kelly clamp. There were

doubtful on admission, positive on February 6, and negative on February 12. A Congo red test showed no retention of dye. Examination of the pus revealed no sulfur granules or fungus. Stains and guinea-pig inoculations showed no tubercle bacilli.

X-ray examination of the chest on admission showed cardiac enlargement, bilateral pleural effusion and increase

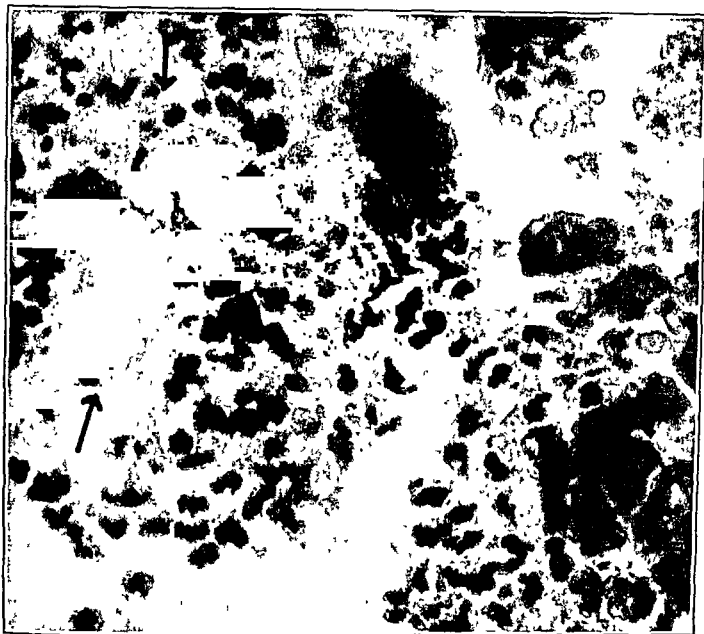


FIGURE 1. Photomicrograph of Granulation Tissue Showing a Cluster of *Actinomyces* ($\times 700$).

rales in the right chest and dullness anteriorly up to the 4th rib. The left side of the chest was clear. There was an apical systolic murmur (Grade III), with a precordial thrill. The abdomen was distended and shiny, and there was an area of flaccidity and sensory loss below an operative scar in the right upper quadrant. The operative scar extended into an abscess involving the abdomen below the liver. The presence of free fluid in the abdomen was suspected but was never proved. The spleen was palpated 4 fingerbreadths below the ribs on the right. The right hip was held in 45° of flexion and could not be straightened. There was suggestive clubbing of the fingers and toes.

Laboratory examination showed a red-cell count of 3,400,000 and a white-cell count of 33,600, with 74 per cent neutrophils, 20 per cent lymphocytes, 4 per cent monocytes and 2 per cent eosinophils. Examination of the urine was normal on admission and remained so throughout the hospital course. Two blood cultures taken shortly after admission were negative. The blood non-protein nitrogen was 25 mg. per 100 cc. and the serum protein was 7.4 mg. Blood Hinton reactions were

in the lung markings in the lower two thirds of each lung field. Portions of the 10th and 11th ribs had been resected on the right.

The patient was studied for the first 5 days, during which time he required several copious dressings to the back each day. The temperature reached 102 or 103°F. each evening, and he was frequently shaken with a severe nonproductive cough.

On the 6th day, incision and drainage of the deepest sinus in the right flank were carried out. A biopsy of this tissue was taken, and pathological examination of the granulation tissue showed "peculiar yellowish brown staining masses with club ends around the periphery, characteristic of actinomycosis."

The patient continued to run a fever and on the 12th day was started on sulfadiazine, 0.5 mg. six times a day. The temperature fell to normal after 5 days of this therapy and remained normal subsequently. The drainage became negligible within 2 weeks. The right leg was put in traction and physiotherapy was given, with gradual return of motion. The sulfadiazine level was followed every 3 or 4 days and remained chiefly between 8 and 12

mg. per 100 cc, the lowest level recorded being 4.5 mg. and the highest 145 mg.

The drug was continued, and after 4 weeks the patient had gained 5 pounds and seemed much better. After 6 weeks the back was dry and epithelialized. The sulfa-

A case of actinomycosis in a nine-year-old boy is presented. The disease was of sixteen months' duration, starting in the chest and extending through the diaphragm into the retroperitoneal space

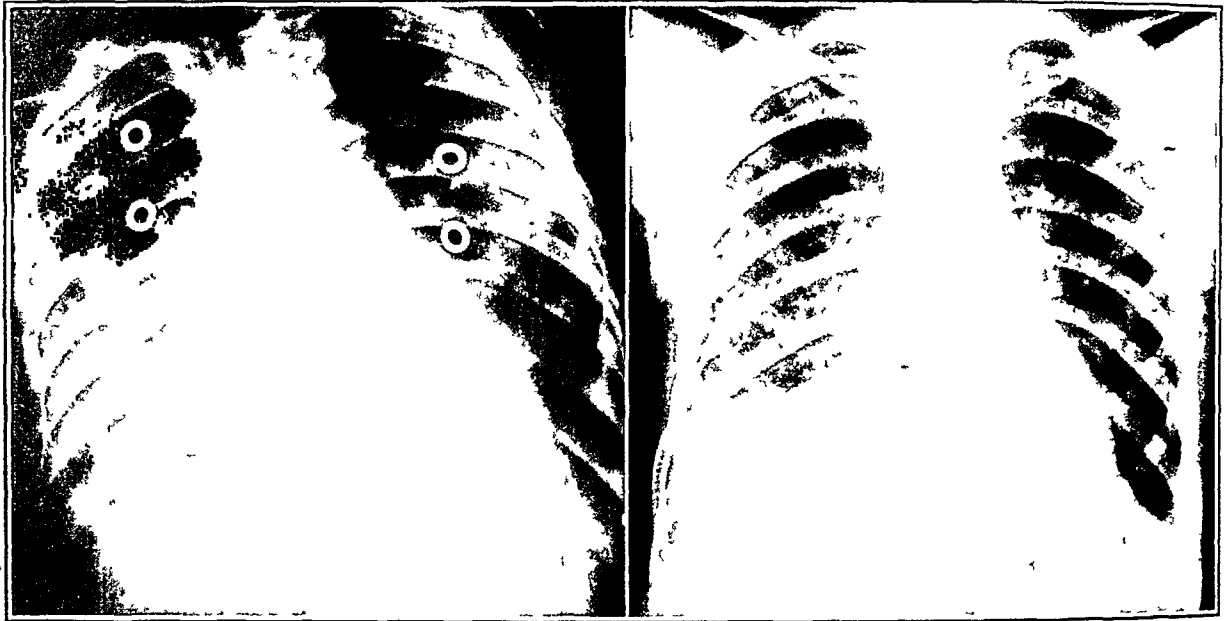


FIGURE 2. Photographs of X-Ray Films of the Chest before and after Treatment.

The film on the left shows actinomycotic involvement of the right lung; that on the right, taken five months later, shows complete clearing.

diazine dose was cut to 0.5 mg. four times a day, but the level remained within the former range. After 8 weeks the patient was walking, and subsequent to this his convalescence was uneventful. He was discharged on May 20, weighing 63 pounds.

For 8 months after discharge sulfadiazine was continued at a dosage of 1.5 mg. daily, and the patient was seen at regular intervals.

On June 16, 5 months after admission and about 1 month after discharge, there were no signs in the chest.

On his latest visit, on February 15, 1943, the patient was not recognizable as the same boy who had been admitted a year previously. He weighed 85 pounds and walked without a limp. The cardiac murmur had disappeared, the chest was clear, and the sinus tracts were well healed. The spleen was no longer palpable, and the liver could just be felt. The weakness of the abdominal wall on the right was still present. X-ray films showed the right diaphragm to be still somewhat raised, but the lungs were normal. The patient was going to school and leading an entirely normal life.

SUMMARY

A review of the literature shows a group of cases of actinomycosis favorably influenced by treatment with sulfanilamide and sulfapyridine.

Treatment with sulfadiazine without other therapy resulted in a rapid cure.

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MEDICAL PROGRESS

THE PLASMA PROTEINS: THEIR IMPORTANCE IN CLINICAL MEDICINE AND SURGERY*

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DURING the past few years a great amount of effort has been devoted to studies of the plasma proteins in health and disease. With the development of satisfactory methods for the preservation of plasma, which has been of great importance in military medicine and which has made plasma widely available to practitioners, the need for an understanding of the functions of the different constituents of plasma is obvious. This report is intended to supplement Loeb's¹ excellent and comprehensive review on the plasma proteins, with a more detailed discussion of their functions and a consideration of methods for the treatment of various types of protein deficiency.

METHODS OF STUDY

Progress in the field of blood proteins, as in most other fields of medical research, is dependent on the chemist. Blood plasma is a complex fluid consisting of a mixture of crystalloid substances and protein in water. The proteins of the plasma comprise a large group of molecular species that differ over a wide range in chemical characteristics and physiological functions. The primary aim in the chemical study of these substances is to separate them into fractions of sufficient purity so that they may be accurately characterized chemically. This aim is now beginning to be realized² on a sufficiently large scale to make it possible to use these fractions extensively in the treatment and study of disease.

In making the different plasma proteins available in a highly purified state, the chemist is providing the clinician and the physiologist with a fundamental tool essential to the satisfactory study of their functions. The importance of having a plasma protein relatively pure is obvious from the standpoint of the therapy of a deficiency of that protein, but its importance for the controlled investigation of its functional significance cannot be overemphasized.

As Loeb pointed out, recent advances in the chemistry of the plasma proteins have been aided by the development of new analytical tools, although methods for the preparation of pure protein fractions in some cases antedated their use. The first of these, the ultracentrifuge, makes it possible to analyze proteins by means of their rate of sedimentation in a centrifuge rotating at a tremendously high rate of speed. The rate of sedimentation depends on the size and shape of the molecule. The second tool, the electrophoresis apparatus, enables the chemist to separate and analyze a mixture of proteins on the basis of their rates of migration in an electric field. This in turn depends on the size, shape and particularly the net charges of the respective molecules. Since the net charge depends on the hydrogen ion concentration of the buffer solution in which the protein is dissolved, it is essential always to know the pH, and particularly the type of buffer used in any analysis.

Tiselius, whose name is borne by the modern electrophoresis apparatus that he developed, divided the plasma globulins into three components—alpha, beta and gamma. Albumin migrates most rapidly, alpha globulin next, then beta globulin and fibrinogen and finally gamma globulin, which exhibits the slowest rate of migration in the electric field. In each of these electrophoretic components of plasma, as in the fractions prepared by salting out with different concentrations of neutral salts, there is not one protein, but a number of different proteins that happen to exhibit a common type of behavior under the particular conditions of the analysis, but that may be further separated under different conditions. The value of both ultracentrifugal and electrophoretic analysis depends to a large extent on the ease and accuracy with which the results can be read, which in turn are due to the fact that a complicated optical system devised for each makes it possible to record the results graphically.

These two tools, which analyze proteins on the basis of quite different attributes of the molecule, have been very useful as guides and checks on the more conventional and important methods of

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gm. of a normal mixture of plasma proteins. It has likewise been demonstrated that the quantitative response to the injection of concentrated albumin solutions is what might be expected from these accurate *in vitro* measurements.²⁹

Although albumin seems to behave in the human circulation as might be expected on the basis of its physicochemical properties, it should not be regarded as an inert substance trapped in the circulation like gum acacia. Rather, it is in a constant state of dynamic equilibrium with the tissue proteins. For example, shortly after the injection of acacia the concentration of serum albumin falls markedly, presumably to compensate for the increase in oncotic pressure produced by the acacia, which cannot be so readily removed from the circulation.³⁰ Furthermore, albumin, and to a lesser extent some of the other serum proteins, are not held completely within the blood vessels, but apparently do pass in small amounts across the capillary walls, as the extensive researches of Drinker³¹ and Landis³² have shown, and even perhaps across the glomerular capillaries, as the work of Dock suggests.³³ Plasma proteins that pass across the capillary wall into the tissue fluid, as well as other proteins derived from the tissues themselves, probably do not pass back directly into the capillaries but are returned to the circulation by the lymphatic system.³¹

Whereas serum albumin plays an important role in the regulation of blood volume, it is not the only factor concerned. If it were, the nephrotic patient would have virtually no circulating plasma, because of the extremely low levels of serum albumin in nephrotic plasma and its low oncotic pressure. Pressure within the tissues themselves, — which rises with the accumulation of edema fluid,³⁴ — the intake of salt and fluids,³⁵ the permeability of the capillary wall, and arterial and venous pressures, all play a role in the regulation of amounts of fluid held within and without the main circulation.

There is nothing to add to the discussion by Loeb¹ on the source of plasma albumin in the body. Considerable evidence implicates the liver and particularly the hepatic parenchymal cells as the main site of albumin manufacture, but it cannot be said that albumin is manufactured *only* by the liver.

Plasma Globulins

Although plasma albumin constitutes a relatively homogeneous group of closely related proteins, the plasma globulins are multiple and complex. As a group, they differ from albumin in their greater molecular asymmetry, lower net charge and, in most cases, larger molecular size.³⁶ The stability of most globulins is less than that of the albumins,

but this is not universally true. In fact, one cannot generalize about the globulins, which are a large group of complex and very different proteins.

Whereas serum albumin is developed early in life, the pattern of serum globulins increases in complexity with growth and development and as a result of the contact of the organism with its environment. Thus, Rapoport and his co-workers³⁷ have recently reported on the plasma protein fractions in the neonatal period and infancy. They have shown that whereas both albumin and globulin concentrations of the plasma are somewhat lower shortly after birth and increase slowly throughout infancy, the increase in the globulin fraction is proportionately greater. How much of this is due to the normal processes of maturation and how much to the response to various antigenic stimuli is not yet clear. This relative hypoproteinemia of early infancy is of interest in relation to the ease with which edema develops in newborn infants shortly after delivery. The following discussion will be confined largely to the importance of the globulins from the functional point of view, which is of interest to the clinician, rather than to their chemical characteristics, which in many cases are still to be defined accurately.

Reactions of immunity. That antibodies are globulins is supported by abundant data derived from the study of both human and animal serums.³⁸ Much of the antibody globulin found in the plasma of the newborn infant is derived from its mother.³⁹ This may be acquired in two ways: by passage across the placenta from the maternal circulation, and by transfer in the colostrum. The latter route seems to be the sole method of transfer of antibodies in certain herbivorous animals such as the cow,^{40, 41} in which the structure of the placenta is such that there is a far less intimate relation between maternal and fetal circulations than exists in the human placenta, with its very thin layer of syncytium and cells separating the two circulations. The placental route of transfer in human beings is almost certainly the more important of the two. Recent studies of the etiology of erythroblastosis fetalis indicate that the passage between the two circulations can be a two-way one, since the mother is immunized by cells derived from the fetus, and her antibodies then return to the fetal circulation, where they produce the destruction of fetal cells and the severe form of hemolytic anemia associated with erythroblastosis fetalis.⁴²

The duration of this inherited placental immunity seems to vary in proportion to the concentration of antibody inherited. Most of this inherited antibody is lost at the end of six months, but during the first six months of life most infants

are protected from scarlet fever, diphtheria, poliomyelitis and measles, provided their mothers possess antibodies to these diseases.³³ On the other hand, infants possess little or no immunity against other diseases, such as pertussis, for which adults do not possess circulating antibodies in an appreciable concentration. It is in the age period from a few months to two years that the mortality of most infectious diseases is highest; that is, during the time between the loss of inherited immunity and the acquisition of active immunity as a result of outside stimuli. The antibody globulin pattern of the adult is gradually built up as a result of the repeated antigenic stimulation of frank infections latent or unrecognized infections and artificial immunization. Before the age of six months, infants, like young rabbits, do not respond well to antigenic stimuli,³⁰ and it is for this reason that active immunization against pertussis, diphtheria and smallpox is usually deferred until the age of six months is reached.

Few specific antibody globulins have been characterized chemically, with the exception of those found in the serums of highly immunized animals, which have been found to be gamma globulins; that is, globulins that migrate slowly in the electric field. Methods for the detection of antibodies have been entirely nonchemical in the past but with the development of quantitative immunologic techniques, the chemist has gradually begun to invade the province of the immunologist.

Although antibodies are extremely useful in the diagnosis of many infectious diseases, and their presence in the serum usually indicates a state of resistance, their primary importance in bringing about the cure of specific infections is in many cases open to question. In general, passive immunization by the administration of sufficient preformed antibody is more universally effective in prevention than in the treatment of infectious disease. Thus, tetanus antitoxin can prevent tetanus when given in sufficient quantities, but its therapeutic effect is dubious. On the other hand, both diphtheria and scarlatinal antitoxins are unquestionably therapeutically effective when administered early in the disease, and the antibacterial serums developed against the pneumococcus⁴³ and the influenza bacillus⁴⁴ have proved their worth in the clinic. In such a disease as typhoid fever, and in most virus diseases, the administration of antibodies is ineffective as a form of treatment, possibly because the etiologic agent multiplies within the body cells,^{45, 46} where it is protected from the action of the antibodies.

Most evidence indicates that the antibody globulins, or at least those globulins produced in response to antigens that gain access to the body from out-

side,* arise in the reticuloendothelial cells. Evidence for this view is not overwhelming but is extremely suggestive.⁴⁷

Besides the antibodies, there are other globulin components of normal plasma that play a role in immune reactions. These are the fractions of complement or alexin, which are of protein nature. Complement has been divided into four components. Two protein components, the so-called "midpiece" and "endpiece," have been separated from guinea-pig serum by Pillemer, Ecker, Oncley and Cohn,⁴⁸ and from human serum by Ecker, Pillemer and their associates,⁴⁹ and have been shown to have mobilities that place them with the alpha and beta globulins. Further studies along these lines should help to elucidate this exceedingly complex field of immunology. There is little evidence on the source of complement, but it is known that this substance is regenerated very rapidly after depletion.⁵⁰ Although there can be no doubt of the importance of complement to in vitro immunologic tests, notably the complement-fixation reaction, there is far less evidence that complement plays any vital role in the resistance of the body to infection. Ham and Dingle⁵¹ have shown that complement is apparently responsible for the hemolysis of a patient's own blood that occurs in paroxysmal nocturnal hemoglobinuria, in which it acts in conjunction with an unidentified hemolysin. Complement action is also known to be essential to the Donath-Landsteiner reaction, and in all probability actually produces the hemolysis of the syphilitic type of paroxysmal hemoglobinuria, after the cells have been sensitized by the cold hemolysin. In both these instances, complement plays an adverse role in the body economy. In vitro it is known to enhance the speed of phagocytosis,⁵² and it is essential to the destruction of gram-negative organisms by the bacteriolysins of the serum, as shown by Spink and Keefer⁵³ for the gonococcus, and by Fothergill and his co-workers⁵⁴ for *Haemophilus influenzae*.⁵⁴ In vitro bactericidal tests carried out in our own laboratory with the beta-hemolytic streptococcus indicate that complement is essential to the bactericidal action of whole blood,⁵⁵ as had been demonstrated in the case of the pneumococcus by Robertson and his associates.⁵⁶ In the case of both these gram-positive cocci, phagocytosis precedes the bactericidal effect. Its importance in vivo has not, however, been clearly shown, but is suggested by some work of Rutstein and his co-workers,⁵⁷ who found that in certain cases of pneumococcal pneu-

*The isohemagglutins probably develop as a result of the maturation process and not in consequence of antigenic stimulation. Study of the chemical nature of these essentially normal antibodies which are readily identified by their activity in agglutinating the red cells of persons of other blood groups should be of great interest.

monia there seemed to be a partial deficiency of complement. That complement titers might fall during acute disease states in which an antigen-antibody reaction is probably taking place is suggested by the finding of low values in serum disease.^{57, 58}

(To be concluded)

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**CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL****Weekly Clinicopathological Exercises**

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**BENJAMIN CASTLEMAN, M.D., *Acting Editor*EDITH E. PARRIS, *Assistant Editor***CASE 29451****PRESENTATION OF CASE**

A forty-nine-year-old mechanic entered the hospital because of substernal pain of one day's duration.

The patient had been in apparent good health until five years before admission, at which time, during the course of a physical examination, an aortic diastolic murmur was discovered. No history of a chancre could be obtained but the suspicion of syphilis was substantiated, however, by a positive serologic test. He was treated regularly for two years, medication consisting of intramuscular injections as well as about six intravenous injections. No other treatment was given until the month before entry when he received five intramuscular injections. Eighteen months before entry he noted moderate fatigue but continued working at his heavy job. One day, about three months before admission, he developed severe crushing substernal pain early in the morning, while sitting and waiting to go to work. Bromoseltzer gave some relief. He worked till the noon hour of that day. The pain recurred while eating lunch. His pulse was said to have been fast. The pain subsided after passing gas by rectum several times after one hour. Five weeks before entry he had recurrence of the same pain while eating; this lasted one or two hours. He continued to work for four days without distress but awakened each night with severe pain and dyspnea. He had difficulty in sleeping for three or four nights because of orthopnea. From this time on he experienced some pain on exertion and eventually stopped working. The blood pressure was said to have been "204 systolic." The radial pulse was 84, but at the "base of the heart" the rate was found to be 160. He was given quinidine, and in about thirty-six hours the radial pulse rate and the heart rate at the base of the heart were said to have responded. An electrocardiogram taken two weeks before admission showed a rate of 90, left-axis deviation, depressed ST segments in Leads 1 and 2 and inverted T waves in Lead 1. Moderate num-

bers of ventricular premature beats were present, at times in pairs, and also occasional auricular premature beats. The day before entry he awoke after two hours of sleep to void. He did not return to bed, and while sitting, he developed the same substernal pain, which was so severe as to necessitate a hypodermic injection by his physician. The day of admission he experienced substernal discomfort on the way to the hospital. He was said to have had no digitalis for one week, and before then one small tablet a day, after taking one three times a day for two weeks.

He had had gonorrhea twenty-six years before admission.

Physical examination showed an obese, apparently healthy man. The pupils were equal and reacted to light. An arterial pulse was visible in the neck. The heart was enlarged to the left, the apex being 13 cm. from the midsternal line in the fifth interspace. The sounds were of fair quality and regular. There was a blowing aortic diastolic murmur and a Grade 2 aortic systolic murmur. The pulse was Corrigan in type. The lungs were clear. The abdominal examination was negative. The deep tendon reflexes were active.

The blood pressure was 180 systolic, 55 diastolic. The temperature was 98.6°F., the pulse 96, and the respirations 25.

Fluoroscopic examination revealed a large transverse heart with a base measuring 9.5 cm. The heart width measured 15.7 cm., as compared with 23.5 cm. for the inner diameter of the chest. In the left anterior oblique view there was a curve in the midthird of the cardiac silhouette that extended out 3 or 4 cm.

The patient was given nitroglycerin on admission, and this was repeated two and four hours later, giving a total of three doses. There was some relief from pain, but morphine was also given because of the severity of the pain. The patient was apprehensive and tense and ate sparingly; he was, however, able to sleep. He received two 0.2-gm. doses of digitalis. Fifteen hours after admission, at about 5:00 a.m., he signaled for the nurse, who found him with his head back, gasping, unconscious and pulseless. He died twenty minutes later.

DIFFERENTIAL DIAGNOSIS

DR. PAUL D. WHITE: We can assume that this patient had aortic regurgitation. At the age of forty-five, aortic regurgitation means either rheumatic heart disease, which is more probable in this part of the world, or aortic syphilis, which is less common here than in many other places. It rarely means anything else, but we did see a patient at medical grand rounds this morning with aortic regurgitation due apparently to hyper-

*On leave of absence

sion—that might be called functional regurgitation, without aortic-valve disease. In the record of this case there is no statement of early dyspnea, nor did the patient complain of paroxysmal tachycardia. Of course, paroxysmal tachycardia due to coronary or myocardial insufficiency may precipitate symptoms not previously present. We cannot be sure of what happened at first in this patient.

When pain did begin its duration was intermediate between what we usually find with angina pectoris on effort (or decubitus) and what we usually find with myocardial infarction.

It is distinctly unusual, although possible, for pain due to coronary insufficiency to occur first at rest and only later on effort. Almost invariably it is the other way around, some weeks, months or years elapsing before the pain finally occurs at rest. Here we have the reverse. I expect that the description of the pain would have been the same throughout. I assume that it was substernal oppressive pain. It is said that the radial pulse rate was 84, but that at the base of the heart the rate was 160. I do not know what was meant by that. There is no further description. Was the heart rate regular? It is important to determine whether the patient had paroxysmal fibrillation, which can give a heart rate of 160 and a radial rate of 84—a very large pulse deficit. Although unusual in this kind of patient, it is possible. It is unlikely that a coupled rhythm would have caused every other beat to have been premature, thus failing to reach the wrist; a bigeminal rhythm is rare with a rate as fast as 160. I do not believe that we can be quite sure what did happen, but the best bet is tachycardia with auricular fibrillation; with tachycardia of other sorts a pulse deficit of this degree usually does not occur.

Quinidine usually is given for arrhythmia, sometimes for tachycardia. Perhaps it was given for both in this patient. Whether the rhythm became normal as a result of quinidine or spontaneously we cannot be sure. There was some arrhythmia later, with auricular premature beats; hence the patient might readily have previously had an auricular tachycardia. Otherwise the electrocardiogram is simply characteristic of a big left ventricle from any cause. Such a big left ventricle is due most commonly either to hypertension or to aortic-valve disease. We know that the patient had aortic regurgitation, and so that fits best—namely, a big heart with aortic regurgitation. Coronary heart disease is one other possibility, but we do not as a rule find left-axis deviation with uncomplicated coronary heart disease. He may have had a combination of heart diseases. He had a systolic blood pressure of 204. There is no clear indication, however, from this electrocardiographic record of any fresh myocardial infarct. That point is rather im-

portant because from the history it is possible that he might have had several myocardial infarcts. Depressed ST segments do not have the same significance from the standpoint of acute myocardial damage as elevated segments, which in Leads 1 and 2 or in Leads 2 and 3 present reasonable evidence of acute myocardial infarction. We find *no* note of precordial leads, which would have been helpful in such a problem.

DR. BENJAMIN CASTLEMAN: They were not taken.

DR. WHITE: There is a possibility of some digitalis effect in the electrocardiogram, although the patient had not had a great deal of digitalis.

This man's height and weight are not given, but obviously the apex impulse was a long distance out. We can assume from physical examination that he had a very large heart.

I should have liked to have a grading of the diastolic murmur, as well as of the systolic. Perhaps it was Grade 3 or 4, somewhat louder relatively than the systolic murmur and a little more in keeping with aortic regurgitation and dilatation of the aorta than with rheumatic, syphilitic or calcareous aortic stenosis. The findings would have been reversed with a loud (Grade 4) aortic systolic murmur, and perhaps a Grade 2 diastolic murmur, if the case were one of rheumatic aortic stenosis. The Corrigan pulse is further evidence of free aortic regurgitation.

The deep tendon reflexes were active. It does not look as if the patient had any obvious evidence of syphilis of the central nervous system to go with the aortic syphilis; both are often present in the same patient.

We have not two readings of the diastolic pressure, which is sometimes recommended in cases of aortic regurgitation. There may be quite a difference between the sound changes in trying to determine the diastolic level. It is often wise, especially in aortic regurgitation, to record two readings. If the sound changes and disappears at about the same time one reading is enough. Not infrequently one will get a diastolic reading of 40 as the sound changes, and zero when it disappears. No one knows which is correct, so far as I am aware. Here we have the one reading of 55; quite likely there was a distinct change in note at that point.

"Fluoroscopic examination revealed a huge transverse heart, with a base measuring 9.5 cm." The base should be much wider to be called wide, if it is the width of the heart in the anteroposterior view that is meant, but if this refers to the cardiac pedicle,—that is, the shadow of the great vessels,—9.5 cm. is distinctly wider than normal. The width across the great vessels is normally 6 or 7 cm. "The heart width measured 15.7 cm., as compared with 23.5 cm. for the inner diameter of the

chest." With reference to the transverse diameter of the heart, the normal in a patient of this size is about 12.5 cm., so that there was at least 3 cm. of enlargement by x-ray.

Now we come to one of the oddities of the case. Everything has gone along easily up to this point "In the left anterior oblique view there was a curve in the midthird of the cardiac silhouette that extended out 3 or 4 cm." That is evidently something unusual. There is no statement about the anteroposterior view.

DR. CASTLEMAN: No films were taken.

DR. WHITE: Then this must have been a fluoroscopic observation; but there is no statement whether the bulge was in front or in back, whether it pulsated or what its action was.

DR. CASTLEMAN: There is no further statement.

DR. WHITE: The point is rather important. I think that fluoroscopy by ourselves might have been helpful in our present dilemma.

This was not an abrupt death—that is, one due to acute coronary insufficiency, such as we find with ordinary angina pectoris and sometimes even with coronary thrombosis. A tamponade or a coronary occlusion could explain it.

Regarding the diagnosis, the presence of both coronary and myocardial insufficiency with pain and dyspnea in a man in the forties with a history of venereal disease, a positive serologic reaction, fairly free aortic regurgitation, a big left ventricle and aorta and early death, indicates almost certainly the presence of syphilitic aortitis with aortic regurgitation, left ventricular weakness and partial occlusion of the coronary ostia. As a matter of fact this history is almost too perfect for syphilitic aortitis with involvement both of the valve and of the coronary ostia. In such cases it is common to have both dyspnea and pain, and the pain is likely to be just as atypical as this—that is, atypical for coronary heart disease, either angina pectoris or myocardial infarction, the pain coming as it did for an hour at a time and not leaving any distinct trace on the electrocardiogram. The only real oddity is the unusual heart shadow by x-ray. It is not quite described as a bulge, but I suppose it would be if it measured 3 to 4 cm. in depth. It is important to remember that the aorta starts in the middle of the heart shadow. The beginning of the aorta cannot be seen in any view by x-ray. The first 2 or 3 cm. are buried in the heart shadow, almost in the center of the heart. Thus some lesion related to the base of the aorta would be the best bet for this unusual shadow. What could it be? An aneurysm at the root of the aorta is, I suppose, the best explanation of that shadow—an aneurysm possibly involving a sinus of Valsalva and extending out in one direction or another or even located just above the sinuses of Valsalva.

An aneurysm sometimes presents itself some distance from the site of origin. A myocardial aneurysm of the left ventricle is lower than this bulge in position and so is unlikely here.

DR. CASTLEMAN: Dr. Currens is here and can answer your questions about the fluoroscopy.

DR. WHITE: How would you describe the bulge, Dr. Currens? Did it pulsate?

DR. JAMES CURRENS: It did not seem to pulsate any more than the rest of the aorta. If there was any pulsation it was transmuted. It was fairly round in contour, that is, it was regular in contour and did not extend out necessarily as a definite discrete mass.

DR. WHITE: Did it seem to be a part of the heart shadow? Could you distinguish it from the rest of the heart shadow except as it came out beyond it?

DR. CURRENS: No.

DR. WHITE: Was it anterior or posterior?

DR. CURRENS: Anterior. It seemed to be above the heart. It was in the region of the aorta rather than that of the heart.

DR. WHITE: It says here that it was in the middle third, but it was probably in the upper third too.

DR. CURRENS: Between the middle and upper thirds, I should say.

DR. WHITE: Could you see the bulge in the anteroposterior view?

DR. CURRENS: Yes; but not nearly so well as in the left anterior oblique view.

DR. WHITE: And the heart otherwise was large? There was no engorgement of the lung hilar shadows?

DR. CURRENS: Not particularly.

DR. WHITE: One other site for a syphilitic aneurysm in that region, which I have never encountered myself, but which is on record, is an aneurysm at the beginning of one of the coronary arteries. However, that is an extreme rarity. When the coronary arteries are involved, they are usually atherosclerotic. They may once in a while be invaded by a dissecting aneurysm of the aorta. There are two cases with involvement of the coronary artery itself without dissection of the aorta that we have tucked away to report sometime. In these cases there was rupture of the coronary artery and hemopericardium secondary to dissection of the wall of the artery. One of them was that of a patient with recent or fresh coronary thrombosis. A definite bulge of the heart shadow could not have been seen by x-ray in those cases.

The other question here concerns the matter of death. If this aneurysm was located in this region, how did the patient die? It is common for a patient with syphilitic aortitis to die by rupture of the aneurysm into either the pleural cavity or the pericardium. It would be quite consistent with

the story here for an aortic aneurysm near the mouth of the aorta to rupture into the pericardium with death in twenty minutes or so. That all seems too easy, however, except for the unusual position of the bulge, which might nevertheless have been an aneurysm.

I have put down other less probable possibilities, but I believe that we should take the diagnosis that I have just presented as the most likely, even though it may not be correct. Syphilitic aortitis plus coronary heart disease could have been the answer—that is, independent conditions, the coronary heart disease having resulted in death.

A hypertensive aorta with dissection into the sinuses of Valsalva, with or without aortitis, and a final rupture into the pericardium might have been the answer. Or even rheumatic heart disease or subacute bacterial endocarditis could explain the aortic regurgitation, with syphilis of the aorta on the side. Neoplasm of the heart is another odd condition that could have been present, or a congenital aneurysm of a sinus of Valsalva. A congenital defect superimposed on a bicuspid aortic valve has been described by Maude Abbott,¹ in which there may be a large sac extending out from the base of the aorta and involving a sinus of Valsalva with dissection of the wall and rupture into the pericardium. If that were present here, and were not due to syphilis, it would be in addition to the syphilitic aortitis.

I think that, despite all these other possibilities, we are probably justified, with what we have here, in diagnosing simply aortic syphilis with aortic regurgitation, marked cardiac enlargement, coronary insufficiency secondary to the syphilitic involvement of the aorta involving the ostia of the coronaries, and an aneurysm at the mouth of the aorta, perhaps involving a sinus of Valsalva, with rupture into the pericardium. Sudden death is possible in syphilitic cases without rupture of an aneurysm, but such a death would be more sudden than is stated here.

CLINICAL DIAGNOSES

Syphilis, cardiovascular, with aortic regurgitation and aneurysm of the ascending aorta.
Congestive heart failure.

DR. WHITE'S DIAGNOSES

Syphilitic aneurysm of aorta, with rupture into the pericardium.
Hemopericardium, with cardiac tamponade.
Syphilitic aortitis, with aortic regurgitation and with involvement of coronary ostia.
Coronary insufficiency.
Cardiac hypertrophy.

ANATOMICAL DIAGNOSES

Dissecting aneurysm of ascending aorta, with rupture into the pericardium.
Hemopericardium, with cardiac tamponade.
Syphilitic aortitis, with aortic insufficiency.
Cardiac hypertrophy, hypertensive.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At autopsy this man had a tremendous pericardial sac that was filled with about 500 cc. of blood producing obvious cardiac tamponade, which was the immediate cause of death. Within the pericardium we found a large aortic aneurysmal sac that contained a fair amount of blood clot, both old and new. This corresponded to the bulge observed fluoroscopically. When the aorta was opened there was obvious evidence of syphilitic aortitis throughout its entire length, with all the classic findings—stellate scarring, linear tree-barking and so forth. About 2 or 3 cm. above the aortic valve was a horizontal rent in the intima communicating with the aneurysmal sac, which was within the media of the aorta. This sac extended distally for 6 or 7 cm. to the opening of the innominate artery and down to the base of the heart, but did not reach the level of the coronary mouths. This sac was therefore a dissecting aneurysm of the aorta that had dissected for a relatively short distance.

I believe that three months before entry he had the initial intimal tear, and because of the syphilitic scarring in the media the progress of the dissection was slow and stopped at the arch, in contrast to the usual rapid dissection through the arch and down into the abdominal aorta. The pressure in the aneurysm increased, since blood was getting in but could not get out, and eventually produced external rupture and death.

DR. WHITE: How far down did the syphilitic process extend?

DR. CASTLEMAN: It extended down to the aortic valve, but the coronary mouths were not involved. The aortitis had produced slight but definite separation of the cusps at their commissures, which accounts for the regurgitation. There was little coronary sclerosis.

DR. WHITE: How much did the heart weigh?

DR. CASTLEMAN: The heart was huge, weighing about 900 gm., and was hypertensive in type.

DR. WHITE: The patient had had quite a number of attacks of pain. Do you think he tore his aorta every time?

DR. CASTLEMAN: No; I think that the distention of the aneurysm as it enlarged was enough to produce pain.

DR. WHITE: It is possible to have angina pectoris when an enlarged heart has a wall so thick that it is not receiving enough blood through the coronary circulation, even though everything is open. Thus angina pectoris may occur without coronary heart disease, due to relative coronary insufficiency. That could be a plausible explanation of much of the pain here. The patient did have hypertension, of course, which helps a little toward the diagnosis of dissecting aneurysm. Do you remember, Dr. Castleman, that in the series of dissecting aneurysms that Glendy, you and I reported the history was generally different from that of this case with respect to pain—usually there was one extremely severe attack of pain at the time of the first rupture and then a few hours, days or weeks later there occurred another attack of pain with death, without these recurrent pains. This case is unusual.

DR. CASTLEMAN: Yes; I think the aneurysm was being gradually built up.

DR. WHITE: But then so were the others.

DR. CASTLEMAN: They were much longer in aneurysms, extending all the way down the aorta and without the increased tension that you have here in the localized dissection.

DR. CURRENS: In light of the anatomic findings this case is of considerable interest to me. The late Dr. Soma Weiss in discussing dissection of the aorta cited dissecting aneurysms that dissect up to a region of syphilitic aortitis and then stop. He had one or two cases of this nature, and it was his impression that syphilis actually predisposed against dissecting aneurysm. The case under discussion is an exception to this thesis.

DR. WHITE: I am impressed by the occurrence of dissection of the aortic wall in just that part of the thoracic aorta—the ascending portion—in which the syphilitic process is the most active. This is in contrast to a few nonsyphilitic cases that I have seen in which the dissection of the aortic wall did stop at the arch because of the marked calcification of the entire descending aorta, whose wall was too hard to dissect. In this case the aortitis may have favored the dissection.

DR. CASTLEMAN: I can recall one case of dissecting aortic aneurysm in which the dissection was apparently stopped by syphilitic scarring in the media.³

REFERENCES

- 1 Abbott M. E. *Atlas of Congenital Cardiac Disease*. 62 pp. New York: American Heart Association, 1936. P. 18.
- 2 Glendy R. E., Castleman B. and White P. D. Dissecting aneurysm of aorta: clinical and anatomical analysis of nineteen cases (thirteen acute) with notes on differential diagnosis. *Am Heart J* 13:129-162, 1937.
- 3 Case 7303. Case records of Massachusetts General Hospital. *New Eng J Med* 225:155-159, 1941.

CASE 29452

PRESENTATION OF CASE

A nine-year-old schoolgirl entered the hospital because of a "stuffed-up nose," coryza, fever and joint pains of six days' duration.

The patient had been in good health until about two weeks before entry, when she developed a cold that "never came to a head." There was no fever or loss of appetite. She felt well. Two days prior to entry she complained of being very cold. Her feet hurt when she walked. Her temperature was 103°F. A systolic murmur was heard for the first time by the family physician. The white-cell count was 18,500, with 77 per cent neutrophils. Urinalysis was negative. The family physician placed her on sulfadiazine, of which she received 160 gr (nearly 11 gm) up until the time of admission. The fever, however, persisted. Her appetite became poor but there was no vomiting or diarrhea. There was pain in the right foot and elbow, the neck and the shoulders, but no definite swelling or redness was seen. Motion in the legs and arms was limited. The day before entry she had several slight nosebleeds, and a moderately severe one on the day of admission. The pain shifted to the left elbow and midarm. On the day of admission she coughed up mucus and blood clots, which appeared to come from the pharynx.

Her tonsils and adenoids had been removed a year prior to admission. She had had measles, scarlet fever, chicken pox, German measles and whooping cough earlier in life. At seven years of age she had had "hives" twice, possibly caused by oatmeal.

Physical examination showed a well-developed and well-nourished child in no distress. Both eardrums were dull and slightly injected. Some blood-stained crusts were seen in the nostrils but no sinus tenderness could be elicited. The posterior cervical lymph nodes were slightly enlarged. The heart was of normal size. The sounds were of good quality and regular; there were no thrills. A blowing systolic murmur was heard at the apex and a short systolic blow at the pulmonic area. The pulmonic second sound was greater than the aortic. There was difficulty extending the left arm completely; the pain could be localized at the elbow and in the midarm.

The blood pressure was 110 systolic, 72 diastolic. The temperature was 104.2°F., the pulse 110 and the respirations 30.

The blood showed a hemoglobin of 14.5 gm and a white-cell count of 15,000, with 85 per cent neutrophils. The urine showed a + test for albumin but was otherwise negative.

X-ray examination of the chest revealed slight increased density of the right lung, suggesting

Public Health Service and Procurement and Assignment Service.

It is my hope that this personal letter will serve to convince the doctors marked available that there is a real need for them to seek a commission in either the Army, the Navy, the Coast Guard or the Public Health Service.

FRANK H. LAHEY, M.D.
Chairman of the Directing Board

War Manpower Commission
Procurement and Assignment Service
Washington, D. C.

War Manpower Commission

PROCUREMENT AND ASSIGNMENT SERVICE FOR
PHYSICIANS, DENTISTS, AND VETERINARIANS

Dear Doctor ———:

I am writing you a personal letter — personal because I do not want it to be taken as a form letter from the Procurement and Assignment Service. I want it to be personal in order that I may convince you that the Army, the Navy, the Coast Guard and the Public Health Service need more doctors. The Navy in terms of its requirements is farther away from what it needs than any other branch of the armed services but we need also to supply more doctors to the Army, the Coast Guard and the Public Health Service. Every doctor who has been marked available should either seek a commission or appeal his classification.

You, as a physician of forty-five or under who has been marked available, will shortly receive a notice asking you to appear for a conference with a group made up of representatives of the Army, Navy, Public Health Service and Procurement and Assignment Service. This group will be able and willing to discuss with you any questions that may be in your mind concerning entering the service and applying for a commission.

I wish to give you my personal word that the Directing Board for the Procurement and Assignment Service assures you, one, that those doctors marked available who can pass the physical examination are needed, and two, that they can be spared where marked available without interfering with civilian care.

In the interests of the national need, will you not at least appear before this board as a man marked available to discuss the problem as it relates to you?

I am certain that you know that I would not write this personal letter unless the need was real and my conviction of its justice established.

Sincerely yours,

(Signed) Frank H. Lahey

FRANK H. LAHEY, M.D.
Chairman of the Directing Board

NOTICES

GREATER BOSTON MEDICAL SOCIETY

A dinner meeting of the Greater Boston Medical Society will be held at the University Club on Wednesday, November 17, at 7 p.m. Mr. William Gailmor, news commentator, Station WHN in New York City, and lecturer and propaganda analyst, will speak on the subject, "Russia's Role in a Postwar World." As an added feature, Lieutenant Commander David B. Stearns, U.S.N.R., will give a short talk entitled, "A Urologist at a Naval Air Station."

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, November 16, at twelve noon. Dr. Henry C. Marble will speak on the subject, "The Care of the Wound."

Physicians are cordially invited to attend.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular meeting of the New England Society of Physical Medicine will be held at the Hotel Kenmore on Wednesday, November 17, at 8 p.m. Dr. William D. McFee will act as chairman.

PROGRAM

Fundamentals in Teaching Galvanic Technic Dr. Harry E. Stewart, president, Junior College of Physical Therapy, New Haven, Connecticut, and chairman, Section of Physical Therapy, Connecticut State Medical Society.

Ionization. Dr. Wilmot L. Marden.

A council meeting will be held at 6 p.m., and dinner in the Empire Room at 6:30 p.m.

NEW ENGLAND HEART ASSOCIATION

The next meeting of the New England Heart Association will be held in the Boston Medical Library on Monday, November 29, at 8:15 p.m.

PROGRAM

Observations on Re-examination of Men Rejected for Military Service for Cardiovascular Reasons. Dr. Paul D. White. Discussion by Drs. Burton L. Hamilton, Henry Jackson, Jr., and Samuel A. Levine.

Report of a Patient with Eisenmenger's Syndrome. Drs. C. Sidney Burwell and Eugene C. Eppinger. Circulation and Respiration During an Episode of Chill and Fever in Man. Drs. Mark D. Altschule, A. Stone Freedberg and Haim Haimovici.

Notes on the Transmission of Cardiac Murmurs Dr. Samuel A. Levine.

Interested physicians and medical students are cordially invited to attend.

NEW ENGLAND OTO-LARYNGOLOGICAL SOCIETY

The regular fall meeting of the New England Oto-Laryngological Society will be held at the Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, on Wednesday, November 17.

PROGRAM

10 a.m.—12 m. Sound Motion Pictures (Mosher Laboratory).

2 p.m. Clinical meeting. Presentation of cases from the Massachusetts Eye and Ear Infirmary.

3 p.m.

Business meeting.

Two Instruments of Value in Tonsillectomy. Dr. Henry H. Amsden, Concord, New Hampshire.

The Significance of Eosinophilia in Rhinology. Dr. Daniel Miller.

(Continued on page 7)

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THE MEDICAL PROFESSION'S RESPONSIBILITY IN THE PREVENTION OF BLINDNESS*

HUGO B. C. RIEMER, M.D.†

BOSTON

ONE of the main objects of this paper is to describe what is being done by the state and federal governments for those suffering from defective eyesight. The family physician is the backbone of the medical profession. His guidance and co-operation are essential in any program of care and prevention of disease. That he should be interested in the prevention of blindness might seem to be outside his professional interest. But is the eye not a part of the human body? And certainly his interest is in the human body.

Interest in the welfare of those handicapped by reason of reduced vision has been greatly stimulated by the advent of the Social Security Act. This law was passed in 1935. It makes provision for the indigent blind by paying to the participating state half of all payments up to forty dollars a month; that is, if the state grants a person forty dollars a month, the federal government reimburses twenty dollars. The state, by accepting the benefits of the provisions of this law, actually becomes a copartner of the federal government in effecting its operation. Since the federal government has assumed a part of the responsibility, it naturally follows that it will participate in carrying out the provisions of this law. The federal government has promulgated certain regulations to make the law more universally applicable to all the states, and to see that provision is made for equitable treatment and distribution of funds to all applicants for and recipients of financial assistance.

In order to facilitate its operation, the Social Security Board, soon after the act became operable, made certain definite recommendations relative to blindness. In the first place, it proposed a definition of economic blindness. Secondly, it required that certain medical data be determined and that they be kept by the state agency for each

applicant for assistance, and further, it suggested that the medical examination be made *only* by an eye physician who holds a certificate of the American Board of Ophthalmology; this enables the state to have an authentic record of each person applying for aid to the blind. It developed a record form covering certain medical data, to be filled out by the eye physician after his examination. Massachusetts used the suggested form until recently, when the Medical Advisory Committee and the director of the Division of the Blind composed a new form that includes all the requirements set up by the Board but is developed in a way that best meets the need in Massachusetts. This form requires an accurate description of each eye, and a statement concerning the primary cause of blindness. The etiologic cause of blindness is required, a factor that eventually will establish authentic data that can be used as the basis of a real prevention program. Finally, the Board suggested the appointment of a trained ophthalmologist to review all medical reports.

Many of the states have appointed specialists to head their medical activities as supervising ophthalmologists. It is the duty of the supervising ophthalmologist to review the medical report of each applicant for blind relief. If the report is incomplete or unsatisfactory, a re-examination is required. When there is a doubt in the mind of the supervising ophthalmologist concerning the facts reported, he requests that the applicant appear before him for examination. In some states medical reports on all blind persons requesting any type of service from the state are required. In New York, medical forms on all blind persons who may become known to any public-welfare department are filed with the Commission for the Blind. These are catalogued so that with the aid of this file studies of any one cause of blindness can be initiated.

*Read at the annual meeting of the Massachusetts Medical Society, Boston, May 26, 1943.

†Consulting surgeon, Massachusetts Eye and Ear Infirmary, instructor in ophthalmology, Harvard Medical School.

It is now becoming possible to get reliable statistics about blindness. This has been made possible by the medical reports required by the Social Security Board. Even though such reports cover only the needy blind, a truer picture of the causes of blindness in this country will be secured. We may even hope in a few years to be getting adequate information concerning the incidence of blindness.

Statistical studies of the causes of blindness are of value only in proportion to the needs, faults and possible preventive and rehabilitative measures that they point out. There is no reason why blindness should not be a reportable condition—reportable to some official state agency as soon as it is established. There should exist in every state an official agency to which blindness in a person, young or old, rich or poor, is reported as it arises, thus giving a true picture of the incidence of blindness that is of more importance than the knowledge of the number of blind adults receiving assistance.

When the medical findings reveal that there is a reasonable chance of restoring sight, every endeavor should be made to persuade the applicant to have his sight restored.

One can say that the subject of blindness and its prevention has wide ramifications, the emphasis being placed in different states on the various phases of work. What is developed in the future will depend somewhat on how official and private agencies have been developed in the various states.

The Massachusetts Division of the Blind, concerned chiefly with the education and rehabilitation of the blind and with the care of the indigent blind, is now greatly concerned with the larger and more important program, the prevention of blindness. In this program, the responsibility rests not only on the ophthalmologist but on the entire medical profession. How well the medical profession performs and carries out the provision of the laws that aim primarily to prevent blindness will be one of the most important factors.

No one will argue that the use of prophylactic drops in newborn infants has not reduced blindness from ophthalmia neonatorum. Statistics have proved without a shadow of doubt that this is true. Within the past year not one case of a baby who was blinded because of this disease has been reported to the Division of the Blind. It becomes more important than ever to be vigilant in such cases, since it is a well-known fact that the incidence of venereal diseases increases in wartime. The law requires a Wassermann or Hinton test of pregnant women, making possible the treatment of syphilis when present in the early

stages of pregnancy not only as a benefit to the mother, but also to prevent the birth of syphilitic offspring who may later develop interstitial keratitis, one of the chief causes of blindness. The law requiring a Wassermann or Hinton test before marriage has the same aim—to prevent the birth of a syphilitic offspring who may later become blind.

When it is realized that communicable diseases and trauma are two of the most important causes of blindness, we will doubtless all agree that something can be done to reduce the number of blind in this category.

It is of interest to note that conservation-of-vision committees of state medical societies have been appointed in the following states: Alabama, Connecticut, Florida, Indiana, Kansas, Maine, Missouri, Nebraska, New Hampshire, New Jersey, Oklahoma, Oregon, Pennsylvania, South Carolina and West Virginia. Special committees under state medical societies, also concerned with conservation of vision, have been appointed in the following states: Delaware, Georgia, Iowa, Minnesota, New Hampshire, South Dakota, Tennessee and Wisconsin. Plans are also under way for the publication of an article in the *West Virginia State Medical Journal* that will discuss industrial accidents, glaucoma, ophthalmia neonatorum and trachoma.

Eleven hundred and seventy-six cases of blindness now receiving aid in Massachusetts have been coded in accordance with the standard classification developed by the Committee on Statistics of the Blind, and the results show that there is need of the following: more care in reporting the etiologic factors of blindness; the early detection of all cases of glaucoma; the detection of diabetes before the devastating effects of this disease become manifest; better care of traumatic cases; and authentic data on hereditary cases.

It has been shown by this statistical study that the causes of blindness correspond in percentages closely to those of other states that have made a similar study.

The first principal cause to be considered is infectious disease, such as diphtheria, gonorrhea, measles, meningitis, ophthalmia of the newborn, scarlet fever, smallpox, syphilis, trachoma, tuberculosis and typhoid fever. Three hundred and seventy-six cases (32 per cent) were found in this category. Of these, 128 (11 per cent) were due to syphilis, 51 (5 per cent) to ophthalmia of the newborn, and 150 (13 per cent) to infectious diseases not specified. This percentage can be greatly reduced, since the effectiveness of chemotherapy has been so well established. It requires greater

vigilance on the part of physicians, and when necessary the seeking of advice from a competent ophthalmologist. By following this plan it should be possible to cut this percentage in half.

Next in importance is trauma. From this cause there were 61 cases, or slightly over 5 per cent. It is true that there will always be some cases of blindness due to trauma, but the present rate is altogether too high. It should be recognized that a perforating injury of an eye may not only cause the injured eye to be blind, but may so affect the other eye from sympathetic disease that the victim becomes totally blind. It is the duty of the medical profession to educate the public in regard to this threatened danger, and to see that such cases receive the care of a competent ophthalmologist. A study by Kerby* of 4739 children who are in schools for the blind in the United States shows that 374 cases were due to trauma, and that in 4 out of 10 of the injured cases blindness followed from development of sympathetic disease in the uninjured eye.

Ninety-three (8 per cent) of the 1176 cases of blindness were due to general diseases. This includes diabetes and hypertensive disease, including the arteriosclerotic degenerative diseases. It may not be possible to accomplish very much with hypertension and degenerations resulting from arteriosclerosis; nevertheless, the early recognition of diabetes is most important. It happens altogether too frequently that diabetes is not suspected until the patient has visual complaints, and when he is examined by his eye physician it is discovered that the underlying cause is diabetes. Such a person should certainly have had proper treatment long before he or she reached this stage, blindness thus being prevented.

It was necessary to classify 463 cases (40 per cent) as having an undetermined cause. This seems a rather high figure, and a more careful investigation and study of the cases might have revealed the etiology of the disease.

In 348 cases (30 per cent) the etiology was classified as unknown. This group included cases of glaucoma, cataract and myopia. In cataract sight is of course often restored by removal of the cataract. Regarding myopia, there seem to be no means at present of checking the progress of this condition. The fact that heredity is a factor in myopia should be recognized. Glaucoma was the cause of blindness in 119 cases (10 per cent). This is usually a symptomless disease of middle life, and is one that the ophthalmologist always has in mind when examining anyone who seeks his advice. Often there is no warning whatsoever of the dis-

ease, since the central visual acuity is lost only in the latest stages. The family physician is the first to be consulted by many so afflicted, and they depend on him for advice. He should be sufficiently acquainted with this disease to give them competent advice. Only a trained ophthalmologist can recognize this disease in its early stages. If this is done, proper treatment and care can avoid blindness.

In 152 cases (13 per cent) the blindness was of prenatal or hereditary origin. It seems to be a reflection on the medical profession that so large a number are blind from these causes. Apparently the only way that this number can be reduced is by educating the public of the danger of transmitting these conditions to their offspring.

This year the director of the Division of the Blind, with the co-operation of the Medical Advisory Committee, has had the following laws enacted in Massachusetts. First is an act relative to recording the treatment of infants at birth. This law requires the physician or hospital medical officer to treat the eyes of an infant within two hours after birth with a prophylactic remedy furnished or approved by the Department of Public Health, and he must record on the birth certificate the use of such a prophylactic. Whoever violates this section is punishable by a fine of not more than one hundred dollars. Second is an act relative to reports of treatment of certain wounds. This act classifies wounds from a BB gun or other air rifle with the firearm or gunshot wounds that must be reported to the Commissioner of Public Safety or to the police authorities of the town concerned. Third is a law making it mandatory to report all cases where the vision is 20/200 or less in the better eye or where the peripheral field of vision has contracted to a radius of 10° or less, regardless of visual acuity.

Prevention of blindness should be the chief interest of all official agencies for the blind and of all other agencies concerned with the welfare and health of the population. This program for the prevention of blindness cannot succeed without the full co-operation of the entire medical profession. There are certain fundamentals on which such prevention work must rest. These are an adequate medical determination of blindness, the early recognition of the potentially blind person, the ability to care for those potentially blind, whether adults or children, in an adequate manner, proper prenatal care, and a proper liaison between official agencies for the blind and other agencies, such as the departments of public health and of public safety, industrial commissions, labor commissions and departments of education.

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*Kerby, C. E. Eye conditions among pupils in schools for blind. *Out look for the Blind* 36:270-276 1942

THE THERAPEUTIC VALUE OF TESTOSTERONE PROPIONATE IN ANGINA PECTORIS*

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ALTHOUGH an acute attack of angina pectoris is readily controlled with nitroglycerin, the treatment available for the prevention of such attacks is unsatisfactory. It has been observed that an increase in arterialization of cutaneous blood results when certain organic diseases of the peripheral blood vessels are treated with the testicular hormone, testosterone propionate.¹ There is also some experimental evidence that androgens and estrogens bring about vasodilatation.² With the hope, therefore, of improving the cardiac blood supply by increasing the collateral circulation or the degree of vasodilatation of the coronary arteries, or both, testosterone propionate has recently been used in the treatment of angina pectoris. Published reports thus far have been uniformly favorable.³⁻⁷ The purpose of this paper is to record the results obtained with this form of therapy in an additional series of cases.

Nineteen patients, ranging in age from thirty-five to seventy years and presenting definite evidence of angina pectoris, were given tri-weekly injections of 25 mg. of testosterone propionate§ (Table 1). Eighteen were treated for four weeks, and 1 for seven weeks. Of the entire group, 16 were men. Nine patients had hypertension (a blood pressure of over 150/90 on repeated examinations). Three of these had a history of coronary thrombosis. Of 9 with normal blood pressures, 2 had had a previous infarction. The remaining case was that of a woman of thirty-nine with rheumatic aortic stenosis and insufficiency. The duration of angina pectoris ranged from one month to thirteen years, averaging six years. Each patient was accustomed to the use of nitroglycerin, and, with two exceptions, used a fairly constant number of pills a day. Reference to the daily nitroglycerin consumption offered some measure of the effectiveness of the therapy. The injections were generally given during the late fall and early winter months, so that observations were made during the time of the year when angina pectoris tends to become especially severe. This is important, for the interpretation of any therapeutic procedure carried out just before the advent of warm weather is

always open to question. In all but 2 cases, no other medication was given concurrently and no change was made in the daily routine once treatment was begun.

Evaluation of the results was based on the patient's estimation of the amount of physical activity he was able to perform without precipitating an attack of pain, and the number of nitroglycerin tablets necessary over a twenty-four-hour period. These observations were recorded at the beginning of, during and at the conclusion of the injections. They were again noted from one to fifteen months later. The degree of improvement was classified as marked, moderate and questionable. When the patient was able to reduce the number of nitroglycerin tablets by two thirds or more, the improvement was considered to be marked. This result was always accompanied by an increased tolerance for physical activity. Moderate improvement was considered to have occurred when there was some, but not marked, reduction in the use of nitroglycerin. Those who reported that they felt somewhat better but were unable to do with a smaller number of pills or to increase their tolerance for effort were looked on as questionably improved.

Marked improvement was noted in 5 of the 19 patients. Two, however, reverted to their former clinical state within six to eight weeks, and 1, after a period of fifteen months, obtained no relief when a second series of injections became necessary. Of the remaining 2 patients, one maintained the improvement for four months, the other for one month. It is apparent, therefore, that of the 5 patients who experienced definite relief only 2 continued to benefit after four months, and in 1 of these the result could not be duplicated when it became necessary to repeat the therapy.

Moderate improvement was observed in 1 case, but aminophyllin was given with the testosterone, and it is also likely that a coronary occlusion took place just prior to medication. Questionable results were obtained in 2 patients, but even that degree of improvement was maintained by only one of them during the subsequent months. Death occurred in the other patient who, although temporarily somewhat improved, was also receiving digitalis and a mercury diuretic.

In 11 patients no change whatever was seen at the conclusion of treatment or at any time there-

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§The testosterone propionate used in this study was supplied by Ciba Pharmaceutical Products, Incorporated, Summit, New Jersey, under the trade name Perandren.

TABLE 1 Summary of Data

Case	Age	Sex	Duration of Angina	Limit of Physical Activity	Before Therapy			Electrocardiogram
					Nitroglycerin Pills Required Daily	Blood Pressure		
	yr		yr					
1	58	M	3	Pain after walking, 100 feet on level ground at rest	no pain	6-8	130/86	Normal
2	52	M	1/10	Pain after walking city block also after shaving, no pain at rest	no pain	6	180/100	Normal
3	65	M	9	Pain after walking 1 or 2 blocks no pain at rest		1-2	190/88	Normal
4	35	M	1/2	Pain when climbing stairs, no pain at rest		3-4	110/80	Normal
5	54	F	1	Pain after walking half a block also with emotional upsets no pain at rest		5-7	180/100	Normal
6	63	M	6	Semi invalid because of pain with the slightest effort no pain at rest		5	138/76	Left bundle branch block, T ₁ and T ₂ inverted
7	63	M	10	Varying amount of effort resulted in pain pain at rest occasionally		4-8	210/120	Diphase T ₁ and T ₂
8	39	F	2	Pain on little effort and at rest		3	130/70	T ₁ inverted
9	50	M	6	Pain with effort and emotion and at rest		3	130/80	Diphase T ₁ and T ₂
10	50	M	1/2	Pain with effort after meals and at rest		2-3	196/126	Sharp inversion of T ₁ and T ₂
11	70	M	12	Pain with little effort no pain at rest		5-8	140/72	Right bundle branch block
12	56	M	6	Pain with little effort and at rest		4-5	170/80	Intraventricular block, T ₁ , T ₂ and T ₄ inverted
13	30	M	4	Pain on effort after meals		0	150/88	Normal
14	50	M	10	Pain after walking half a block		1	130/78	T ₄ sharply inverted
15	42	M	2	Pain on walking		5-6	118/78	Normal
16	60	M	13	Pain climbing stairs and at rest		2	145/80	Normal
17	66	M	12	Pain after walking half a block		2-3	126/80	Right bundle branch block
18	55	M	7	Pain on walking up incline		1-2	220/110	Normal
19	40	M	6	Pain with varying types of effort		3-4	108/75	Normal

Case	Therapy Received	After Therapy			Results
		Nitroglycerin Pills Required Daily	Blood Pressure	Follow Up Period	
				mo	
1	10/9/42	1-2	170/60	4	Marked improvement original symptoms returned after 2 months
2	11/13/42	6	200/120	4	No improvement
3	11/23/42	1-2	178/78	2	No improvement
4	12/4/42	3-4	110/80	3	Questionable improvement, felt better for 2 months
5	12/9/42	5-7	200/100	3	Questionable improvement continued to feel somewhat better
6	1/14/43	0	140/60	3	Marked improvement, 1 month later developed pneumonia after which gained weight and energy
7	3/1/43	4-8	240/100	1	No improvement
8	3/15/43	3	128/78	1	No improvement
9	9/20/42	3	130/76	2	No improvement
10	3/22/43	1-2	190/120	2	Aminophyllin also given, coronary occlusion probably occurred just before therapy moderate improvement for 1 month
11	11/1/42	5-8	126/70	4	No improvement
12	1/12/43	4-5	156/100	1	Died 1 month after treatment was finished
13	10/14/42	0	140/80	4	Marked improvement which has been maintained
14	3/11/43	1	140/90	1	No improvement
15	8/1/42	1	120/70	1	Marked improvement
16	9/1/41 12/1/42	5-6	140/76	16	Marked improvement after first series no improvement after second
17	1/18/43	2-3	130/80	2	No improvement coronary occlusion 2 months later
18	3/10/43	1-2	210/110	1	No improvement
19	2/2/43	1-4	108/75	2	No improvement

after. One of these developed a coronary occlusion two months after the injections were completed.

No changes in the blood pressure or electrocardiogram were observed in any case and no toxic effects or significant changes in libido were noted. The behavior of this entire group was not unlike what would be expected in following any average series of cases of angina pectoris over a short period of time, one patient having died unexpectedly and another having developed an acute coronary thrombosis.

The difficulty of appraising therapy in the treatment of angina pectoris is perhaps best illustrated by the history of one of the patients in this group. Thirteen years ago, R. S., then forty-seven years of age, had been seen by one of us (S. A. L.) and diagnosed as having coronary artery disease and angina pectoris. At that time he could not walk a city block without experiencing the crushing substernal oppression so characteristic of angina. During the following twelve years, while receiving no specific form of therapy, there was considerable spontaneous improvement so that it was not unusual for the patient to walk miles without pain. Obviously this improvement could have been credited to any treatment used at the beginning of that period. Over a year ago, when the attacks of angina again became very frequent, testosterone was administered and considerable relief was noted. Recently, however, another course of injections failed to duplicate that result. May not this entire sequence of events reflect the vagaries of angina pectoris rather than the true effect of any therapeutic agent?

SUMMARY

Testosterone propionate in doses of 25 mg. three times a week was given to 18 patients with typical angina pectoris for four weeks, and to 1 patient for seven weeks.

In all but 2 cases the patients received no other medication and continued the daily routine to which they had been accustomed.

Of the 19 patients, 9 were hypertensive and 1 had rheumatic aortic stenosis and insufficiency. Five had had a previous coronary occlusion.

Results were judged by the amount of physical activity necessary to produce an attack of angina, and the number of nitroglycerin tablets used daily. The degree of improvement was classified as marked, moderate and questionable.

Five were markedly improved at the conclusion of the treatment. Two, however, reverted to their former clinical state within six to eight weeks, 1 obtained no relief from a second series of injections after fifteen months of comparative comfort, and 1 has been followed for only one month. One patient was moderately improved, 2 questionably improved, and the remaining 11 obtained no benefit.

No change in the blood pressure or electrocardiogram and no toxic effects were noted.

Realizing that the clinical course of angina pectoris may vary a great deal spontaneously, we are unable to conclude that testosterone propionate has any beneficial therapeutic effect in this disease.

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THE TREATMENT OF RHEUMATOID ARTHRITIS WITH GOLD*

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ALTHOUGH the history of the use of gold salts in the treatment of rheumatoid arthritis is extremely interesting and unusual, it will not be recounted here since it has been so adequately summarized by Cecil and his collaborators.¹ It is interesting, however, to note that the use of gold in arthritis probably owes its origin to Mollgaard, who in 1927 thought that this precious metal had value in the treatment of tuberculosis. Some French students of arthritis believe that tuberculosis is the causative agent in the rheumatoid form of this disease, and this may well have suggested to Forestier² the use of gold salts in the treatment of arthritis.

Gold is unique also in that it is practically the only form of therapy among the many hundreds suggested for the treatment of arthritis that has had consistently favorable reports. The fact that it was slow to gain favor, particularly in this country, was due to the obvious toxic properties of the agent and its untoward effects. That these are still large factors seems to be evidenced by the facts submitted by all the writers on the subject and will be prominently emphasized in this report.

PHARMACOLOGY

This study has not brought to light any positive facts concerning the action of gold salts in alleviating the symptoms of rheumatoid arthritis. Whether its action is bacteriostatic,³ shock-producing,⁴ immunologic to joint structures⁵ or stimulating to the reticuloendothelial system⁶ still remains in the realm of theory.

Physiologic facts in respect to the fate of gold after injection into the human body are quite well established. Freyberg, Block and Levey⁷ and Block, Buchanan and Freyberg⁸ have shown that colloidal gold and colloidal gold sulfide are poorly absorbed and that more gold per gram of tissue is found in the liver than in the kidney, and have found that the feces are the chief route of excretion. In the case of crystalline preparations (gold sodium thiomalate, gold sodium thiosulfate and sodium succinimide aurate), more gold was found in the kidney per gram of tissue than in the liver, and during the time this preparation was used most of the gold was excreted in the urine.

Experimentally, the site of the primary pathologic lesions following the administration of these

substances occurs in the organs where the greatest deposition of gold occurs.⁹ That this is also the case in human beings seems to have been borne out clinically. Another feature of importance is the large percentage of gold salt that is retained in the organism for months before elimination is complete.¹⁰

GOLD PREPARATION AND METHOD OF THERAPY

The gold salts used in this study were limited exclusively to aurothioglucose,[§] and the maximum dosage in any one course was 1.24 gm., given over a period of fifteen weeks. Ten-milligram, 25-mg and 50-mg. doses were given intramuscularly semi-weekly for two weeks each, and 100-mg. doses were given weekly for nine weeks. A second course was never begun until after a six-week period had elapsed. Many of the cases received two courses and some of them three. The second course was repeated no matter what the result had been after the first, unless there had been untoward effects or reactions contraindicating such procedure.

CLINICAL MATERIAL

The type of case used in this series was to a large extent governed by the type of patient attending the clinics from which the material was obtained. The Arthritis Clinic of the Philadelphia General Hospital derives the greatest part of its case load from indigent chronic patients who have had the disease for some time and have made the rounds of hospitals. This is also true, to a great extent, of the clinic at the Jefferson Hospital although a great number of patients are referred there by physicians. The latter patients may be on an economic scale slightly above that of the patients of the Philadelphia General Hospital clinic but the type of case does not appear to differ a great deal. Thus most of the cases were far advanced (Table 1) and had received at some time or other throughout the course of their disease all types of treatment.

The usual study consisted of a complete physical examination, including a complete blood count, urinalysis, and determination of the sedimentation rate (Westgren), as a routine. Other studies were done as indicated. Further sedimentation rate determinations were made at the termination of each course of treatment and before the beginning of the next. Weekly blood-cell counts and

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§Aurothioglucose in the form of Solganol B Olearum was supplied by the Schering Corporation, Bloomfield, New Jersey, through the courtesy of Dr. William H. Steiner.

urinalyses were done. There is no description of the urinary findings, since the reports were almost invariably negative. Occasionally a tran-

TABLE 1. Duration of Disease at the Beginning of Treatment.

DURATION	NO OF CASES	PFR CENT
Under 1 year	8	6
1 year	30	25
2-4 years	28	23
5-9 years	32	26
10 years or over	24	20
Total	122	

sient albuminuria was noted, but otherwise there was little of significance.

One patient developed a leukopenia (a white-cell count below 4000), and the fact that after treatment was stopped and liver extract administered intramuscularly a complete recovery ensued made routine blood-cell counts worth the effort. There was no appreciable change in the hemoglobin level or the red cell count. Many hundreds of determinations were made.

In all the cases an increased sedimentation time was a prerequisite for gold therapy (Table 2).

TABLE 2. Sedimentation Rates at the Beginning of Treatment.

SEDIMENTATION RATES	NO OF CASES
mm /hr	
Below 9	0
9-15	5
16-20	5
21-30	29
31-40	20
41-50	10
51-60	14
61-70	5
71-80	4
81-90	5
91-100	14
101 or over	11
Total	122

With the use of the Westgren method, 8 mm. per hour was considered as the upper limit of normal.

All the cases were polyarticular. Two showed spondylitis deformans. To the student of this disease it will be quite obvious that one rarely finds rheumatoid arthritis involving but one joint and at the same time fulfilling all the necessary criteria for diagnosis.

The cases were grouped according to a functional classification that has been used in our clinics for some time in the study of arthritic patients. It is as follows:

Class 1. Patients presenting the subjective picture characteristic of atrophic arthritis, with duration less than six months and with no demonstrable changes in the joints by clinical or roentgenologic examination.

Patients presenting the subjective picture characteristic of atrophic arthritis, with duration less than one year and joint changes demonstrable but of a moderate degree. There is usually complete subsidence following the removal of foci and adequate therapy.

Class 2. Patients with typical joint changes in one or more groups of joints. The changes are more or less permanent in character but of such a nature that activity is only slightly limited.

Class 3. Patients in whom joint changes have advanced to such a degree that physical activity is greatly limited.

Class 4. Patients with joint changes of such a nature that dislocations, ankyloses and contractures cause total disability. The patient must of necessity be confined to a wheel chair or to bed.

With this classification in mind, it will be noted that only cases of rheumatoid arthritis were in-

TABLE 3. Grade of Disease According to Age.

AGE	CLASS 1	CLASS 2	CLASS 3	CLASS 4	TOTALS
35					
1-20	0	1	1	0	2
21-30	0	5	8	0	13
31-40	1	2	17	1	21
41-50	0	6	24	1	31
51-60	0	8	5	3	36
61-70	0	1	6	10	17
Over 70	0	0	1	1	2
Totals	1	23	82	16	122
Percentages	1	19	67	13	

cluded in this study. Hypertrophic arthritis was not considered. The distribution of grades by ages is shown in Table 3.

TOXIC REACTIONS

The following is a list of untoward reactions reported as due to gold therapy.¹¹

Skin:	Liver:
Erythema	Hepatitis
Exanthema	Jaundice
Papular eruption	Acute yellow atrophy
Desquamation	
Morbilloform rashes	Respiratory tract:
Urticaria	Cough (gold bronchitis)
Exfoliative dermatitis	
Eyes:	Kidneys:
Conjunctivitis	Mild transient albuminuria
Mouth:	Uremia
Metallic taste	
Anesthesia of tongue	Central nervous system:
Transient loss of taste	Eighth-nerve deafness
Dysphagia	
Sore tongue and gums	Hematopoietic system:
Ulcerative stomatitis	Epistaxis
	Purpura hemorrhagica
	Aplastic anemia
	Agranulocytosis
Genitourinary tract:	
Weight loss	
Nausea	
Vomiting	
Epigastric distress	
Diarrhea	

Hartfall and Garland¹² reported 45 per cent toxic reactions in 100 cases. Later Hartfall et al¹³ reported 900 cases with 52.5 per cent toxic reactions. Crawford¹⁴ treated 27 cases with 44 per cent untoward reactions. Sashin and Spanbock¹⁵ had 18 per cent toxic reactions in 22 cases, and Parr and Shipton¹⁶ 26 per cent in 70 cases. Key et al¹⁷ 63 per cent in 44 cases, Snyder et al¹⁸ 15 per cent in 145 cases, and Ellman et al¹⁹ 27 per cent in 90 cases.

One cannot doubt that gold therapy is dangerous in the hands of the average physician when one glances at the long list of untoward reactions that have been reported in the literature. Much of this, however, is avoidable when reasonable care is taken. The purpose of this study is not only to add to the already long list of statistics but to contribute what is believed to be a simple method to reduce the incidence of untoward reactions. It has been suggested that large amounts of vitamin C be used.²⁰ It is, however, agreed that there is no scientific basis for this except perhaps that since most of the untoward reactions are reflected in the skin and mucous membranes it might be wise to attempt to decrease the capillary permeability with vitamin C. Therefore as adjuncts to the gold therapy, the patient was instructed to take 16 ounces of fruit juices as well as a minimum of $\frac{1}{4}$ pound of liver three times weekly. Any unusual signs or symptoms that might develop between visits were to be reported. The patient was especially warned to report itching of the skin, sore mouth or rash, regardless of severity.

Untoward reactions regardless of severity or whether or not attributable to gold were cause for interruption of treatment. Frequently, treatment was again begun when the reaction subsided. Reactions were treated by intramuscular injections of 4 units of crude liver extract three times weekly.

In Table 4 are listed the untoward reactions encountered in this study. In the group of 122 cases that received but one course of gold therapy reactions occurred in 12 cases (9.8 per cent). In the 38 cases receiving two courses, 7 (18 per cent) had reactions, and in the 16 cases receiving three courses, 1 case (6 per cent) had a reaction. Thus in one hundred and seventy six series of injections, reactions occurred in 20 cases. The table also shows the total dose of aurothioglucose received when the reaction became manifest.

RESULTS OF THERAPY

The results of any therapy employed in the treatment of arthritis are always extremely difficult to evaluate. The student of the disease is

frequently hard pressed to classify results in the single case. Factors that create this situation are the wide variance in susceptibility to pain and

TABLE 4 Untoward Reactions

One course	Reaction	Dose, mg.
Myalgia	10 cases	940
Leukopenia	below 5000 cells	270
Generalized erythema	1 case	740
Itching	1 case	190
Cerebral hyperpnea	1 case	740
Mucoridiasis	1 case	840
Maculodermatitis	1 case	440
Lacrimation	1 case	290
Purpura	1 case	340
Stomatitis	1 case	140
Proteinuria	1 case	290
Untoward reactions		
Symptoms	1 case	940*
Severe erythema	1 case	140
Herpetic jaundice	1 case	740
Itching	1 case	940
Thrombocytopenia and ecchymoses	1 case	640
Ulcerations of the pharynx and tonsils	1 case	505
Leukopenia	1 case	340
Two courses		
Seborrheic dermatitis	1 case	90†

*Plus 1740 mg. (first course)

†Plus 249 mg. (first and second courses)

discomfort the patient's psychic response to having someone take an interest in his plight and the resulting euphoria of some patients when under this influence. One must also consider the inherent tendency of rheumatoid arthritis to have natural remissions. All these must be dealt with and kept in mind when trying to evaluate results. In this study a simple classification of improvement has been attempted, and the cases have been divided as follows:

- Group 1 No change. No response whatsoever.
- Group 2 Improved. Few if any objective changes but definite subjective improvement evidenced by the patient.
- Group 3 Markedly improved. Both subjective and objective improvement, diminution of swelling and pain and ability to raise the arms above the head or to walk with or without aid.
- Group 4 Very markedly improved. Marked diminution or complete relief of all subjective and objective symptoms. In some of these cases there remain some stiffness and soreness.

From the tables it appears that there was improvement of a sort in 87 per cent of the cases. If one were to consider the improvement in Group 2 as of questionable nature, since the patient's own statements were the only guide, there remain 53 per cent that were benefited by this form of therapy.

As has been reported by others, there was generally a reduction in the sedimentation rate. Table

5 shows that 78 per cent of those patients receiving one course of treatment manifested a reduction in sedimentation rate. A reduction was noted in exists, even for many years, if pain is still present and the sedimentation rate is elevated, the patient should be given the benefit of gold therapy. If

TABLE 5. Results of Treatment According to Changes in Sedimentation Rate.

THERAPEUTIC RESULTS	RATE REDUCED TO NORMAL				RATE REDUCED 50 PER CENT OR MORE				RATE REDUCED LESS THAN 50 PER CENT				RATE UNCHANGED				RATE INCREASED				ALL CASES	
	I*	II	III	TOTAL	I	II	III	TOTAL	I	II	III	TOTAL	I	II	III	TOTAL	I	II	III	TOTAL		
Group 4 (V M I)	6	1	0	7	21	4	1	26	14	2	1	17	6	1	0	7	3	3	0	6	63	36
Group 3 (M I)	0	1	1	2	6	2	0	8	9	0	2	11	1	1	1	3	1	4	1	6	30	17
Group 2 (I)	3	0	1	4	13	2	1	16	19	4	0	23	7	2	1	10	3	4	1	8	61	35
Group 1 (N C)	0	0	0	0	0	1	1	2	3	0	2	5	2	0	1	3	1	3	1	5	15	9
Worse	0	0	0	0	0	1	0	1	2	0	0	2	2	0	0	2	0	2	0	2	7	4
Total†	9	2	2	13	40	10	3	53	47	6	5	58	18	4	3	25	8	16	3	27	176	
Percentage‡	7	5	12		33	26	19		38	16	31		15	11	19		7	42	19			

*Roman numerals refer to courses
†Of total in any one course

47 per cent of those patients receiving a second course and in 62 per cent of those receiving the third course. At the end of the first course of gold 7 per cent of the patients showed an increase in sedimentation rate. In spite of this, many of the patients were improved.

Whether or not the gradual reduction in sedimentation rate has any bearing on the rate of improvement one cannot say. However, it would seem so until one examines those patients whose sedimentation rate showed no change or was even increased at the end of a course of treatment, when one finds that improvement existed without favorable change in this test.

Table 6 shows the sedimentation rates before and after treatment in the 38 cases receiving two or three courses of treatment.

Table 7 lists the therapeutic results according to the duration of the disease. It will be noted that in the majority of cases the disease existed for more than one year. Almost 70 per cent of the patients were afflicted for more than two years and 45 per cent for more than five years. This series consisted of only 8 patients with rheumatoid arthritis of less than one year's duration. Although the improvement in these cases was marked, the series is not large enough to agree with the finding of other investigators that the earlier the case, the better is the prospect of recovery. Twenty-four patients suffered for more than ten years. Of these, 33 per cent showed subjective improvement, 25 per cent were markedly improved, and 25 per cent were very markedly improved after one course of treatment. Two cases showed no change and 2 were actually worse. These findings are extremely significant in view of the average opinion among physicians that cases of this type should be considered hopeless. Whenever rheumatoid arthritis

the result can only be classified as "improved," it will have been worth the effort.

Table 8 lists the results of treatment according to age groups. The majority of patients ranged

TABLE 6. Sedimentation Rates before and after in 38 Patients Receiving Two or More Courses of Therapy.

CASE NO.	COURSE I			COURSE II			COURSE III		
	BEFORE	AFTER	RESULTS	BEFORE	AFTER	RESULTS	BEFORE	AFTER	RESULTS
1	34	12	V. M. I.*	14	12	I.			
2	64	41	I.	47	80	N. C.	86	80	N. C.
3	75	15	M. I.	15	15	I.			
4	58	10	V. M. I.	50	78	I.	65	54	N. C.
5	95	75	I.	70	75	W.			
6	26	16	I.	16	31	W.			
7	36	16	V. M. I.	13	13	M. I.	18	32	N. C.
8	53	30	M. I.	10	37	N. C.			
9	50	31	V. M. I.	37	18	V. M. I.			
10	38	2	V. M. I.	45	70	V. M. I.			
11	60	10	I.	32	15	I.			
12	60	18	V. M. I.	25	15	V. M. I.			
13	50	50	V. M. I.	30	10	V. M. I.			
14	28	40	V. M. I.	45	29	V. M. I.	37	30	V. M. I.
15	95	40	V. M. I.	85	75	I.	88	85	N. C.
16	40	28	M. I.	40	38	V. M. I.			
17	70	35	I.	35	13	V. M. I.			
18	35	18	V. M. I.	16	8	V. M. I.			
19	115	69	V. M. I.	70	35	V. M. I.			
20	100	70	V. M. I.	70	31	V. M. I.			
21	35	16	I.	17	10	I.	53	37	M. I.
22	28	27	I.	55	120	I.	105	106	M. I.
23	43	28	M. I.	27	100	W.	90	65	N. C.
24	10	10	I.	55	20	I.	25	20	M. I.
25	24	14	I.	9	20	I.			
26	30	23	M. I.	23	30	I.			
27	22	10	V. M. I.	10	18	V. M. I.			
28	25	23	I.	26	38	I.	18	105	M. I.
29	19	14	M. I.	10	90	V. M. I.	19	13	M. I.
30	28	55	V. M. I.	70	100	M. I.			
31	88	25	I.	85	25	I.			
32	75	55	M. I.	5	15	M. I.	59	16	M. I.
33	27	40	I.	20	112	N. C.	9	2	I.
34	40	20	I.	30	25	I.	43	20	V. M. I.
35	17	10	I.	6	40	M. I.			
36	45	15	M. I.	7	44	M. I.			
37	50	20	V. M. I.	37	18	I.	70	35	I.
38	95	90	I.	28	100	M. I.	112	110	I.

*The abbreviations correspond to those used in Table 5.

between thirty-one and sixty years of age. It will be noticed that the age of the patient was no contraindication to treatment with gold, since the re-

sults obtained were essentially the same as those in the younger age groups.

COMMENT

In our experience in two large arthritis clinics over a period of more than fifteen years, no form of therapy has been encountered that offers so

courses of gold therapy. It is likewise borne out that more than one course of treatment is necessary to maintain relief. However, not so much improvement should be expected from subsequent treatment as one is apt to get from the first one.

Ignoring those cases that showed only subjective

TABLE 7. Results of Treatment According to Duration of Disease.

THERAPEUTIC RESULT	DURATION UNDER 1 Yr				DURATION 1 Yr				DURATION 2-4 Yr				DURATION 5-9 Yr				DURATION 10 Yr OR OVER				ALL CASES	
	I*	II	III	TOTAL	I	II	III	TOTAL	I	II	III	TOTAL	I	II	III	TOTAL	I	II	III	TOTAL	NO.	PER CENT
Group 4 (V, M, I)	4	0	0	4	15	4	0	22	8	1	0	9	14	5	2	21	6	1	0	7	63	36
Group 3 (M, I)	1	1	0	2	3	4	2	9	5	2	1	8	2	1	2	5	6	0	0	6	30	17
Group 2 (I)	1	0	0	1	8	3	1	12	12	3	3	18	14	2	0	16	8	4	0	12	61	35
Group 1 (N, C)	0	0	0	0	1	1	0	2	2	0	1	3	1	1	3	5	2	2	1	5	15	9
Worse	0	0	0	0	0	0	0	0	1	1	0	2	1	1	0	2	2	1	0	3	7	4
Totals	8	1	0	9	30	12	3	45	28	7	5	40	32	10	7	49	24	8	1	33	176	
Percentages†	7	3	0		25	32	19		23	19	31		26	26	41		19	21	6			

*Roman numerals refer to courses
†Of total in any one course

much promise in the treatment of rheumatoid arthritis as does gold therapy. Many of the cases presented have been treated in these clinics and elsewhere for many years without benefit, the therapy consisting of removal of foci of infection,

improvement, 54 per cent of those receiving one course and 53 per cent of those receiving three courses showed both subjective and objective improvement.

The incidence of 9.8 per cent of untoward reac-

TABLE 8. Results of Treatment According to Age of Patient.

THERAPEUTIC RESULT	LESS THAN 21 Yr				21-30 Yr				31-40 Yr				41-50 Yr.			
	I*	II	III	TOTAL	I	II	III	TOTAL	I	II	III	TOTAL	I	II	III	TOTAL
Group 4 (V M I)	1	0	0	1	-	3	0	10	8	0	1	9	11	4	1	16
Group 3 (M I)	0	0	0	0	0	1	0	1	2	2	3	7	5	0	0	5
Group 2 (I)	1	0	0	1	5	0	2	7	9	2	0	11	12	7	2	21
Group 1 (N C)	0	0	0	0	1	0	0	1	2	2	2	6	2	0	0	2
Worse	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	2
Totals	2	0	0	2	13	4	2	19	21	6	6	33	31	12	3	46
Percentages†	2	0	0		11	11	12		17	16	38		25	32	19	

*

	51-60 Yr				61-70 Yr				Over 70 Yr				ALL CASES	
	I	II	III	TOTAL	I	II	III	TOTAL	I	II	III	TOTAL	NO.	PER CENT
Group 4 (V M I)	1	4	0	21	4	1	0	5	1	0	0	1	63	36
Group 3 (M I)	8	2	2	12	4	1	0	5	0	0	0	0	30	17
Group 2 (I)	8	3	0	11	6	0	0	6	1	2	1	4	61	35
Group 1 (N C)	1	0	2	3	2	1	0	3	0	0	0	0	15	9
Worse	2	2	0	4	1	0	0	1	0	0	0	0	7	4
Totals	36	11	4	51	17	3	0	20	2	2	1	5	176	
Percentages†	30	29	25		14	8	0		2	5	6			

*Roman numerals refer to courses
†Of total in any one course

vaccines, filtrates, snake venom, sulfur, vitamins, physiotherapy, artificial fever and so forth.

As has been reported by other writers, there is a decided tendency toward a reduction in the sedimentation time—78 per cent of 122 cases receiving one course, 47 per cent of those receiving two courses, and 62 per cent of those receiving three

tions in individuals receiving but one course of treatment is significantly lower than that reported by other authors. However, the incidence was twice as great in those receiving two courses, but there was only 1 such case in these 16 patients receiving three courses. The grand total of 11 per cent of untoward reactions in 176 courses of gold

therapy suggests a distinct reduction in the incidence noted by other investigators. With but one exception, reactions were not manifested until the patient had received at least the 50-mg. doses. When it is considered that 100 mg. has been advocated as an initial dose, it is understandable that a greater incidence of untoward reactions might occur. In this study, three factors are thought to have been responsible for the reduction of toxic reactions: namely, the use of large doses of fruit juices for vitamin C, the use of liver for vitamin B complex and extreme caution in the consideration of untoward reactions.

Age does not appear to be a contraindication to gold therapy. Significant changes in the blood were observed in only 1 case. Likewise, there were no important changes in the urine.

SUMMARY

A series of 122 patients receiving a total of one hundred and seventy-six courses of 1.24 gm. of aurothioglucose intramuscularly is reported.

The results of all courses of treatment were as follows:

Thirty-five per cent showed only subjective improvement, 17 per cent were much improved, 36 per cent were very much improved, 9 per cent showed no change, and 4 per cent were worse.

The percentage of untoward reactions was 9.8 per cent during the first course, 18 per cent during the second, and 6 per cent during the third, an incidence of 11 per cent in one hundred and seventy-six courses of therapy.

A simple method for the reduction of untoward reactions is suggested.

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MEDICAL PROGRESS

THE PLASMA PROTEINS: THEIR IMPORTANCE IN CLINICAL MEDICINE AND SURGERY (Concluded)*

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Clotting process Fibrinogen is classified as a plasma globulin and is the soluble precursor of fibrin, which makes up the matrix of a blood clot. The fibrinogen molecule has properties that make for elasticity and a firm clot. It is a long slender molecule exhibiting double refraction of flow.² Its source is in all probability the liver, but it can apparently be manufactured with such rapidity that only overwhelming hepatic damage will lead to a deficiency of plasma fibrinogen. This is occasionally seen in acute yellow atrophy and in carbon tetrachloride poisoning. A few cases of congenital fibrinogenopenia have been described.⁵⁰ Such deficiencies of fibrinogen are of little clinical significance because of their rarity.

On the other hand, two other globulins concerned with the clotting process are of great clinical importance, as recent work has shown. The first, prothrombin, is the precursor of thrombin, which, according to the classic clotting theory, is produced from prothrombin by the influence of calcium and thromboplastin derived from tissue juice or the breakdown of blood platelets. Prothrombin and thrombin apparently have the mobilities of beta globulins. Prothrombin is present in the circulation in considerable amounts under ordinary circumstances, but a marked fall in plasma prothrombin concentration occurs under certain clinical conditions, notably severe hepatic damage and severe obstructive jaundice. In the first case, the hypoprothrombinemia is apparently due to the failure of the liver to synthesize this protein⁶⁰ (it should be noted that the liver is again implicated), in the second case, the deficiency is not due to a primary failure in synthesis but to a failure of absorption of fat soluble substances in general, of which vitamin K is one.⁶¹ Vitamin K is apparently essential to the synthesis of prothrombin by the liver.⁶² If it is injected or given by mouth with bile salts to promote its absorption, there is a prompt restoration of the blood prothrombin level if hepatic function is adequate.⁶³

These discoveries are of great importance in biliary surgery, since one of the chief hazards of operations on cases of severe obstructive jaundice in the past was abnormal bleeding. In addition, the recognition of hypoprothrombinemia in cases of hemorrhagic disease of the newborn,⁶⁴ which may be prevented in some cases by the administration of vitamin K to the mother before delivery, is another important practical advance.⁶⁵

Since clinicians are interested not only in treating defective clotting but also in producing controlled defects in clotting, the work on dicoumarin^{66, 67} should be followed with interest. The use of this powerful drug, which seems to act specifically on prothrombin, in the treatment of thrombosis, has been delayed by the lack of suitable means of controlling the clotting defect once it is initiated. Hence, Davidson and MacDonald's⁶⁸ paper on the effectiveness of synthetic vitamin K₁ oxide in dicoumarin hypoprothrombinemia will be of great importance if further studies confirm their work.

The second globulin important in blood coagulation has been brought to light by the work of Tagnon, Taylor, Lozner and their associates. Nolf originally proposed that clotting is brought about by a proteolytic enzyme in the plasma that can produce clotting, or when present in larger amounts, lysis of clots.⁶⁹ Such an enzyme may be produced from plasma by treating it with chloroform. In addition to Nolf's work, which has been confirmed by Tagnon and his co-workers,^{70, 71} Taylor and his associates⁷² have for some years been interested in the substance that is deficient in hemophilic blood. This thromboplastin substance is definitely a globulin,⁷³ but its more accurate chemical characterization has not yet been carried out. This substance disappears fairly rapidly from hemophilic blood after administration, but it can be injected either in purified form or as fresh plasma, and temporarily rectifies the clotting defect of hemophilic plasma. It is of great interest that chloroform treatment of the globulin fraction, which rectifies the hemophilic coagulation defect, gives rise to a proteolytic enzyme.⁷⁴

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§For those interested in the complexities of blood coagulation and in the evidence for Nolf's interpretation of the experimental data, his review⁶⁹ is recommended.

Catalytic agents. As Salter⁷⁵ has recently pointed out, many of the most physiologically active and important substances are of a catalytic nature, and hence are present in very small amounts in the blood. Enzymes and hormones fall into this group. Chemical research has indicated that most enzymes are of protein nature, with prosthetic groups that confer on them their special properties. Minute but measurable amounts of certain enzymes such as amylase, alkaline and acid phosphatase circulate normally in the plasma. Marked increases in concentration have been found to characterize certain pathologic conditions, such as the rise in serum amylase that is found in acute pancreatitis.⁷⁶ The hormones, derived from the pituitary and thyroid glands, are likewise active agents present in minute amounts, probably in the globulin fraction of the plasma. None of these substances are ordinarily considered with the plasma proteins, but their presence in plasma is pointed out to emphasize its complexity.

Pressor substances. In recent years it has become apparent that, in addition to the elevation of blood pressure produced by adrenalin in emergencies, another humoral mechanism exists that can elevate blood pressure in response to renal ischemia.⁷⁷ This field has been confused by the fact that the two chief groups of workers have introduced different terminologies. However, the fundamental facts are these. Renin, an enzyme and probably a globulin, is liberated from the kidney under various conditions that produce renal ischemia. It does not itself elevate blood pressure, but acts on a substrate ("hypertensinogen"⁷⁸ or "renin activator"⁷⁹), which is one of the plasma globulins, to produce the true pressor substance ("hypertensin"⁷⁸ or "angiotonin"⁷⁹), which is probably a polypeptide. Although this humoral mechanism of hypertension has not been demonstrated in cases of human hypertension, it seems likely that it may explain those cases of hypertension that are definitely due to renal disease. Hypertensin or angiotonin has a number of interesting physiologic effects on the circulation that are under active investigation.⁸⁰

Abnormal globulins and hyperglobulinemia. A number of disease states are characterized by an increase in the globulin fraction of the plasma. The normal value for plasma globulin is from 2.0 to 2.5 gm. per 100 cc., and in some diseases this may rise as high as 6 or 7 gm. In many cases, but not always, this hyperglobulinemia is associated with hypoalbuminemia, so that the total protein value is a resultant of the two tendencies. Hyperglobulinemia may be due to an increase in the normal globulin constituents of the plasma, to

the presence of abnormal globulins or to both. Gutman and his colleagues⁸¹ have made a careful study of the plasma proteins in multiple myeloma, a disease characterized by extremely high plasma protein levels, and have shown that some cases are characterized by increases in different fractions of the normal serum globulins and some by abnormal globulins, one of which is the Bence-Jones protein, which appears in the urine and is characterized by its peculiar solubility behavior when heated. In addition to multiple myeloma, certain types of liver disease, particularly cirrhosis of the liver, are associated with hyperglobulinemia and the presence of abnormal globulins, and a number of chronic infectious diseases likewise manifest hyperglobulinemia. Of these, the commonest are the tropical diseases, particularly kala azar and chronic malaria; the chronic relapsing diseases thought to be due to allergy, such as acute nephritis, rheumatic fever, disseminated lupus erythematosus, periarteritis nodosa and dermatomyositis; lymphopathia venereum, which exhibits strikingly high plasma globulin levels; and a number of other chronic infectious diseases, such as subacute bacterial endocarditis and tuberculosis.⁸¹

Acute nonspecific responses to infection. One of the most interesting fields for speculation and study on the role of the plasma proteins is the response of the body to acute infection. The studies of Tillett, Francis, Avery, Abernethy and others have shown that there is a chemical fraction of the pneumococcus, the so-called "C carbohydrate," to which a group of rather peculiar immune reactions can be demonstrated in many acute infections, not necessarily pneumococcal in nature. Anti-C substance precipitins appear in the serum shortly after the onset of pneumonia and other acute infectious diseases, and disappear soon after recovery, unlike most antibodies that are specific and appear only after recovery. These antibodies manifest themselves by the appearance of a positive skin reaction to the C substance, which is intermediate between the immediate and delayed types, reaching its maximum in about eight hours.^{82,83} They differ from ordinary antibodies also in that precipitation of the C substance takes place only in the presence of calcium ions.⁸⁴ Further studies of this peculiar antibody have shown that, unlike other antibodies that are normally found in the gamma globulin fraction, it seems to be present in the alpha globulin fraction,⁸⁵ a fraction of serum that has been shown by Longsworth and his colleagues⁸⁶ to increase during the acute stage of acute infectious diseases. Furthermore, it has been shown by immunologic methods⁸⁷ to be a protein not present in normal serum.

Possibly related to this interesting alpha globulin is the discovery of Tillett⁸⁸ that any febrile illness results in a rapid increase in the bactericidal power of the patient's serum for certain strains of beta-hemolytic streptococci, and that this bactericidal power disappears shortly after the subsidence of acute symptoms. This bactericidal property of the serum has been shown by Tillett and Stock⁸⁹ to be associated with a globulin fraction. Of equal interest is Menkin's^{90, 91} recent discovery of the leukocytosis-promoting factor, which can be detected in the serum of animals with acute abscesses and can be concentrated from inflammatory exudates derived from animals and human beings. This factor is likewise a globulin,⁹² and its connection with the other responses to acute infection is one that invites speculation and further study.

Undoubtedly this catalogue of the physiologic significance of the various globulins present in normal and pathologic human plasma is far from complete, but it serves to illustrate the complexity of plasma. Just as changes in the albumin fraction, and to a much lesser extent in the globulin fraction, reflect changes in the state of protein nutrition of the body, so changes in the amounts of the various globulins reflect changes in the constantly shifting equilibrium of the organism with its environment, changes which, although recognized by alterations in the plasma, are fundamentally due to alterations in the activities of different groups of tissues and cells.

TREATMENT OF DISTURBANCES OF THE PLASMA PROTEINS

It should be clear from the foregoing discussion that alterations in the normal pattern of the plasma proteins are not diseases in themselves, but are merely reflections of more deep-seated changes in the body tissues. Therefore, treatment in most cases is not directed at the plasma protein disturbance itself, but at the underlying disease, except where alterations in the plasma, such as the hypoproteinemia of nephrosis, affect the whole organism adversely.

Hyperproteinemia

Hyperproteinemia, which is almost always hyperglobulinemia, is associated with diverse clinical conditions, the etiology of many of which is unknown, but for certain of which, such as kala azar, malaria and lymphopathia venereum, there are definite methods of treatment. Since hyperproteinemia per se has not yet been demonstrated to be harmful, its treatment at present would be unnecessary, even if the proper procedure were known. In a disease like hyperthyroidism the metabolic disturbances are related to the over-

production of thyroid hormone, which is circulating in the plasma. The absolute amounts of hormone, however, are so small, since it acts as a catalytic agent, that one does not think of hyperthyroidism as a specific type of hyperglobulinemia to be treated by suppression or removal of the organ giving rise to the globulin.

Hypoproteinemia

In contrast to excesses, deficiencies of the many plasma proteins are amenable to treatment, which is frequently required to correct serious disturbances of the body economy as a result of the deficiency of circulating protein itself or the underlying functional defect that it reflects. Two general lines of therapy are open to the physician: first, substitution or replacement therapy; and second, provision of adequate protein-forming materials or the stimulus to synthesis, thereby enabling the body to repair its own deficiency. The latter method is always preferable wherever possible, since it offers permanent rather than temporary relief. It takes time, however, and depends on the integrity of the synthetic processes, so that in acute emergencies, or where there is failure of synthesis, replacement therapy must be used.

A deficiency of *circulating total protein* is associated with the rapid loss of blood or plasma, such as occurs in hemorrhage, severe injuries and burns, although the *plasma protein concentration* and distribution may be normal. If the total amount of blood or plasma lost is so great that compensatory vasoconstriction is ineffective in maintaining the peripheral circulation, there occurs the marked fall in blood pressure characteristic of severe shock. Such a condition should be anticipated and prevented if possible by replacement therapy before collapse occurs. The capacity of the body to compensate for blood or plasma loss is conditioned by its ability to manufacture new plasma protein. This occurs at a remarkably rapid rate, provided an adequate circulation is maintained. Following a venesection of 15 to 20 per cent of the total blood volume a normal subject can replace the lost blood with new plasma in about three days.⁹³ Obviously, this is too slow to bring about recovery in traumatic shock, which may become irreversible in a few hours, and furthermore, it has been shown that plasma protein production in dogs is practically nil when the blood pressure is at shock levels.⁹⁴ It is because of this vicious circle that the early treatment of shock with fluids capable of maintaining blood volume is so important. Crystalloid solutions are too rapidly lost from the circulation and tend to lower the plasma protein concentration by dilution and by increasing the rate of plasma loss at the site of injury.⁹⁵ Foreign colloids, such as acacia,⁹⁶

pectin⁹⁷ and gelatin,⁹⁸ have been used successfully to improve the circulation in such emergencies. The ideal replacement fluid, however, is that which most closely approximates that which is being lost. Thus, whole blood or a mixture of whole blood and plasma are best for wounds combining hemorrhage and trauma, whereas plasma is superior for crushing injuries, peritonitis and burns, where the factor of hemorrhage is minimal. Since the blood has a wide margin of safety in its oxygen-carrying capacity, it is usually possible to substitute plasma for blood for the sake of convenience in the emergency treatment of shock. This is the basis for the Red Cross Army-Navy dried plasma program, which provides a therapeutic agent that can be transported in the field without refrigeration and administered without cross matching. Since the effectiveness of plasma in restoring blood volume depends chiefly on its albumin content, the administration of sufficient albumin should be as efficacious as plasma in most shock cases. Because albumin is extremely soluble and stable it has been put up in concentrated form—25 gm. in 100 cc. of saline—to provide an instantly available, compact blood substitute for emergency use under military conditions, where space is at a premium.¹⁰ In clinical trials this has been shown to be effective,⁹⁹ but since it draws on the tissue fluids to increase the volume of circulating plasma, additional water and salt must sooner or later be given the patient by some route (per os, per rectum or parenterally), particularly in cases in which dehydration is present.

Hypoalbuminemia

Hypoalbuminemia, or a diminution of the albumin concentration below normal, gives rise to edema when the value for plasma albumin falls below 2.0 to 2.5 gm. per 100 cc., and is known to be associated with poor healing of surgical wounds, and even with wound disruption after operation.^{100, 101} Hypoalbuminemia is a manifestation of a poor state of nutrition of the tissues in general. Thus, the maintenance of an adequate level of serum albumin is undoubtedly of equal importance in the treatment of medical and of surgical patients. The causes of hypoalbuminemia are excessive loss of albumin, such as occurs in nephrosis or repeated tappings, excessive utilization, as in febrile illness, and inadequate production due to poor protein intake, poor absorption or failure of albumin synthesis. Any one or a combination of these factors may operate in any particular case. Replacement therapy requires large amounts of injected proteins. As Elman and his group¹⁰² have shown dietary nitrogen loss or gain in dogs is distributed between the tissue and serum proteins in a ratio of about 30:1. The protein stores

of the tissues must be replenished as the value for plasma albumin is restored to normal. Clinical experience has shown that this may take considerable time.

Wherever possible, the administration of protein-building material rather than simple replacement therapy should be undertaken. The patient should be put on a high-protein diet, with adequate calories in carbohydrate and fat to spare protein catabolism.¹⁰³ Where the appetite is poor, intravenous alimentation with a protein digest or an adequate amino acid mixture may be used to supplement the oral protein intake. This type of therapy is just coming into its own,^{104, 105} but there are still some practical difficulties in the intravenous injection of a sufficient amount of protein hydrolysate to maintain nitrogen balance. With surgical patients who cannot take any food by mouth, the addition of intravenous protein hydrolysates and parenteral vitamins to the conventional therapeutic regime of saline solution and glucose should do much to improve the postoperative course.¹⁰⁶ Unfortunately, there are some patients, particularly those with liver disease, in whom the synthetic processes are so impaired that replacement therapy with plasma may have to be given if the hypoalbuminemia is to be relieved. The enormous amounts required and the poor ultimate prognosis where liver function is seriously deranged make the value of such therapeutic efforts somewhat dubious. The favorable reports of Patek and Post¹⁰⁷ on improvement in some cases of cirrhosis of liver treated with a diet rich in proteins and the vitamin B complex suggest that definite return of the ability to synthesize albumin may occur on such a regime and that this is the procedure of choice in chronic liver disease. In acute hepatitis, the use of plasma to help tide a patient over a critical period of hypoalbuminemia may be indicated, since the ultimate outlook is fairly good.

It should be pointed out that the amounts of plasma protein required for the therapy of nephrotic hypoalbuminemia are large, since the deficiency of albumin is so extreme and the rate of loss in the urine so high. Until there is a better understanding of the fundamental disturbance in the nephrotic syndrome, however, some form of replacement therapy will have to be used in those patients whose edema does not respond to those simple measures or to those unknown factors that lead to diuresis in some patients. Binger and Goudsmit¹⁰⁸⁻¹¹⁰ have persistently advocated gum acacia in the treatment of nephrotic edema. There seems little doubt of its effectiveness in certain cases, and it has one great advantage over plasma protein—it is retained longer by the kidney and produces an increase in blood colloid. Unfortunately, acacia is deposited in the viscera, particularly the liver,

and may interfere with protein synthesis for that reason.¹¹¹ Hence, its use cannot be recommended. Concentrated human serum¹¹² and concentrated human albumin¹¹³ have both been advocated. Use of the latter, particularly in aqueous solution, is rational; even though the amounts required are extremely large. Protein hydrolysates and amino acid mixtures provide means of increasing the supply of protein-forming material to nephrotic patients and have a role in the treatment of patients with good renal function, as Farr, Emerson and Futcher¹¹⁴ have shown. In cases with poor renal function, the injected amino acids result in a rise of blood nonprotein nitrogen.¹¹⁵

Hypoglobulinemia

Deficiencies in certain globulins do occur and in certain cases can be rectified by appropriate therapy. The antibody globulins are frequently deficient, particularly in infants, since specific antibodies are probably not acquired except as a result of the stimulus of artificial immunization or from contact with the disease-producing agent. In many cases such contacts do not give rise to frank disease, but to latent infection or the carrier state, which may be equally effective in establishing immunity and stimulating antibody production.

Passive immunization is a form of replacement therapy whereby a specific antibody is supplied by injection of the serum from an immune person or an immunized animal. The use of heterologous antibody carries with it the risk of serum sickness, in which the lesions of periarteritis nodosa have recently been demonstrated.¹¹⁶ Because the risk of serum disease is obviated, there is an increasing use of human serum for passive immunization, particularly in the prophylaxis of measles and pertussis and in the treatment of pertussis and scarlet fever.¹¹⁶ The widespread use of whole-blood or plasma transfusions in infants with severe infections is based on the premise that the increased resistance of an adult is associated with an appreciable amount of circulating antibody that may be transferred to the infant. Although, as already pointed out, this is probably the case, studies analogous to those of Lyons on immuno-transfusion for hemolytic streptococcus infections are needed to put this practice on a more rational basis.¹¹⁷

Unfortunately, the fact that even human serum is not without its dangers has been forcibly brought home by the recognition of homologous serum jaundice. Recent studies indicate that this is probably due to a virus present in the blood of patients in the pre-jaundice stage of infectious hepatitis.¹¹⁸ Fortunately, such cases had been

comparatively rare in the United States, although cases have possibly gone unrecognized¹¹⁹ until experience with yellow fever vaccine containing a small amount of icterogenic human serum brought this matter to the fore.¹²⁰ On the other hand, in England, where epidemic jaundice has been relatively common in recent years, many cases of the transfer of jaundice to patients by the injection of human serum, particularly convalescent measles and mumps serum, have been observed.¹²¹ It is to be hoped that all clinicians using human blood, plasma and serum will keep careful records of the lot used, since this is essential for tracing the origin of the icterogenic agent when jaundice develops. The incubation period of this type of jaundice is from one to four months, so that unless a careful history is taken in all cases of jaundice the connection with an injection of human blood or its by-products may be overlooked. Studies on how to eliminate this danger are urgently needed.

The superiority of the method of therapy that depends on supplying the body with protein-forming materials is nowhere better illustrated than in the case of the antibodies. Here the protein-building material is easily supplied by the diet, but the stimulus to antibody formation must be provided by active immunization, which gives rise to a much more permanent and solid immunity than can be achieved by passive immunization. Cannon¹²² has suggested that in severe protein deficiency the ability of the body to form antibodies may be impaired. The results of his further studies will be awaited with interest, since they may have an important bearing on the health of the malnourished populations of Europe in the coming period of reconstruction.

Complement deficiencies, as already pointed out, are rare, but deserve further study.⁵⁸ It is possible that the occasional salutary effect of blood or plasma transfusion in severe infections is due not only to the passive transfer of antibodies or to the supply of some of the needs of the body for protein but also to the passive transfer of pre-formed complement. Experimental studies in animals¹²³ have suggested the necessity of an adequate vitamin C level for complement activity, but subsequent experiments have failed to substantiate this in man.^{124, 125}

Deficiency of clotting substances is frequently encountered in the clinic, usually owing to hypoprothrombinemia, but rarely, in cases of overwhelming liver damage, to fibrinogenopenia as well and, in cases of hemophilia, to lack of so-called "globulin substance." For the provision of these important globulins by replacement, fresh

or adequately preserved plasma must be used.¹²⁶ Either frozen or dried plasma is adequate, with preference for the frozen material, but commercial liquid plasma is inadequate, since it is kept under conditions that destroy the activity of these labile globulins and complement. Better than replacement therapy is the stimulation of prothrombin production by the administration of vitamin K. This is not usually successful where there is extensive liver damage. Unfortunately, no way of curing the coagulation defect of hemophilia other than blood or plasma transfusion is known, and the effect of such therapy lasts but a short time.

* * *

It is probable that the time may soon come when it will be possible to analyze protein deficiencies in terms of their individual components, and to supply the missing components in pure and highly concentrated form. It should, however, be emphasized that replacement therapy is a temporary measure, absolutely essential for acute emergencies, such as shock, acute infections and hemophilic crises. Equally important is the gathering of knowledge concerning the source and essential factors for the synthesis of the different functionally important plasma proteins. Again one is driven back to thinking about the functions of the tissues that are reflected in the pattern of the plasma proteins. In the case of prothrombin, the discovery that vitamin K is essential to its synthesis by the liver has made possible the rational treatment of prothrombin deficiency. Similar studies with regard to the other blood proteins—the essential dietary factors and amino acids necessary for their manufacture—should yield fundamental knowledge of great practical significance in clinical medicine and surgery.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 29461

PRESENTATION OF CASE

A thirty-eight-year-old librarian was admitted to the hospital because of chills, fever and weakness of two weeks' duration.

About seventeen years before entry the patient began to have intermittent attacks of diarrhea and melena that occurred at varying intervals of weeks to several months and lasted several days. During the attacks she was "rundown" and weak, while between the attacks she was quite normal jaundice. The attacks were not related to diarrhea and melena. Two weeks before entry she had a similar chill. She became progressively feverish, weak and tired, and developed generalized malaise. There was a sharp pain in the right lower anterior chest on eating or on deep inspiration. The pain did not radiate.

Physical examination showed a well-developed but thin, pale, feverish, dehydrated woman in no acute distress. The tongue, palate and pharynx were injected and coated with a white exudate. Chest expansion was limited by pain over the liver anteriorly. There were decreased breath sounds over the right base posteriorly. Transient rales were heard over both bases. The heart was of normal size, and the sounds were of good quality and had normal bowel movements. Eleven years before admission she had an attack lasting for several weeks following which an ileostomy was performed. Her general condition improved and the ileostomy worked satisfactorily, requiring attention only about three times daily. Fecal discharge from the ileostomy was semisolid. Bowel movements from the rectum occurred about twice daily, except for brief bouts of increased frequency (five to ten a day) that occurred only about three or four times a year and lasted only one or two days. At these the stools were occasionally bloody but usually consisted of pink-staining mucus. She had an attack of chills and fever at intervals of several months. These lasted only a few hours and then subsided completely. There were associated malaise and occasional vomiting, but no

ity and regular. A blowing apical systolic murmur was heard. The abdomen was soft and tympanitic, with "normal bowel sounds." Moderate tenderness was present over the left flank. The ileostomy appeared to be functioning well, but the surrounding tissue was red and macerated.

The blood pressure was 110 systolic, 58 diastolic. The temperature was 103°F., the pulse 120, and the respirations 28.

Examination of the blood showed a red-cell count of 2,760,000, with 6.2 gm. hemoglobin. The white-cell count was 45,900, with 95 per cent neutrophils. The blood chloride was 89.1 milliequiv. per liter. The nonprotein nitrogen was 24 mg. per 100 cc., and the protein 6.2 gm. One blood culture was negative. A second blood culture showed proteus bacilli that overgrew gram-positive cocci in pairs and diphtheroids. The urine had a specific gravity of 1.018 and showed a ++ test for albumin. The stools were guaiac negative.

Fluoroscopic examination of the chest showed that the motion of the right diaphragm was limited—about 0.5 cm.; the left moved normally. The right diaphragm was elevated. The liver was thought to be slightly larger than usual. There were several linear areas of atelectasis in the right lower lobe just above the diaphragm. There was also an area of increased density, measuring about 3 by 5 cm., apparently above the diaphragm. On the anteroposterior projection a shadow of decreased density was seen through the liver shadow, but this was not present in the lateral view. There was no fluid in the right base.

The patient was given daily intravenous infusions of 2000 cc. of 5 per cent glucose in physiologic saline solution and large doses of vitamins. On the second day she was given 5 gm. of sodium sulfadiazine, followed by daily doses of 25 gm. She received several transfusions. Her condition, however, became progressively worse. Despite a blood sulfadiazine level of 10 to 12 mg. per 100 cc., the temperature remained above 102°F. for the first two days, during which time she had two chills. For the next five days the temperature ranged between 100 and 105°F., with almost daily chills. The pulse varied between 90 and 150 for the first ten days. The patient became progressively weaker and slightly icteric. X-ray examination of the chest on the eighth day showed the previously described area of increased density in the right lower chest to have increased in size. The serum bilirubin was 3.0 mg. per 100 cc. direct and 3.4 mg. indirect. A repeat van den Bergh two days later revealed the serum bilirubin to be 3.8 mg. per 100 cc. direct, and 5.3 mg. indirect.

During the second week the patient had fewer chills. The temperature remained between 101

*On leave of absence.

and 103°F. The pulse gradually rose to 150. She became dyspneic and cyanotic, and a gallop rhythm developed. The respirations became more difficult. The patient became comatose and died on the fifteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. WYMAN RICHARDSON: I see no reason to doubt the fact that this patient had chronic ulcerative colitis for which she was given an ileostomy, apparently with considerable improvement. In spite of the fact that she had this illness before the Chicago Fair, it is possible for one to have amebic disease even though one does not go to fairs. I shall bring that point up again in a moment.

Beginning with the premise that she had chronic idiopathic ulcerative colitis and that this had gone on to bring about her death, I should like to start the discussion with the total white-cell count, which was very high—46,000. One thinks of causes that will produce as high a white-cell count as that and they are not too numerous, especially in an adult. They are, in general, infection, infarction and tumor. We probably can rule out leukemia of the obvious type on the basis of the blood picture, but if we take these three things, infection, infarction and tumor, and consider them from the point of view of this case, we can get some help from this white-cell count. In infection there is, as you know, a polymorphonuclear leukocytosis that is almost 100 per cent in severe infections. In this case there is said to have been 95 per cent neutrophils; the other 5 per cent are not quoted but were undoubtedly lymphocytes. If there were monocytes, my argument would not hold water very well. Massive infarction, on the other hand, will also produce a very high white-cell count. As you know, patients with mesenteric thrombosis may have a total white-cell count higher than this. In these cases of massive infarction, however, the leukocytosis is much more nearly a total leukocytosis, with increase not only in the polymorphonuclear cells but also in the lymphocytes and monocytes, so that the differential picture is much more nearly like that seen in normal blood. This is not just talk because it has been possible to differentiate infarction and infection by examination of the smear alone. This count therefore tends to militate against massive infarction. Tumor, particularly bronchiogenic carcinoma or carcinoma of the liver, may also produce leukocytosis or a leukemoid blood picture, but in these cases, more often than not, one finds a blood picture showing marked evidence of red-cell regeneration, presumably when the marrow is involved, and one is not so likely to see the complete polymorphonuclear leukocytosis that one does in in-

fection. Also, there are qualitative changes in the cells, which I shall not discuss because we have not the smear before us, and also because I have recently emphasized this too much in discussing other cases. So the evidence from this finding alone is that this patient had infection, rather massive infection with large areas of tissue destruction because of the very high white-cell count. I might add if there is not a considerable area of tissue destruction, and if there is not either a large abscess or many small ones, one does not obtain a great increase in the white-cell count. In a septicemia without abscess formation, even acute septicemia or acute endocarditis, the white-cell count is often at a normal or less than normal level.

I believe that the blood chloride was low because of the diarrhea and sweating.

I shall comment briefly about the bilirubin. The patient was definitely icteric, and the direct reaction of the van den Bergh test was in great preponderance over the indirect, that is, the total percentage of direct bilirubin was about 85. This suggests obstructive jaundice.

If one takes this picture and forgets the x-ray examination for the moment, it seems to me that we have a patient with ulcerative disease of the bowel, and that she very likely developed—as so frequently happens—a thrombophlebitis or pyelophlebitis, which could have involved the system of veins that go to the liver, with the subsequent development of either a single abscess or probably multiple abscesses of the liver. One should consider the possibility of subdiaphragmatic abscess. That still is a possibility, but it would not account for the jaundice. If one explains the jaundice on the basis of liver abscess it seems to me that there is evidence in favor of multiple abscesses, possibly associated also with a low-grade infection of the small ducts, a cholangitis. This is rather definite evidence against subdiaphragmatic abscess. One other bit of evidence is the lack of fluid above the diaphragm, which so often occurs in subdiaphragmatic abscess. There are no data from this record that enable me to rule out amebic abscess, but I believe that it was adequately ruled out. One would ordinarily have to keep that in mind.

I have reached the point where I shall call this liver abscess, probably multiple, with perhaps at least one large one. I should like to stop there, but unfortunately there is a 3-by-5-cm. mass in the chest that does not seem to be readily explained.

DR. MILFORD SCHULZ: I do not see the mass on this film. All I can see can be explained by an elevated diaphragm and atelectasis.

DR. CHESTER M. JONES: That is what the doctor who took care of him thought.

DR. SCHULZ: There is no fluid in the chest that I can see. The liver is enlarged.

DR. RICHARDSON: What about the area of decreased density?

DR. SCHULZ: I cannot see that either. This is a gas bubble in the stomach. Someone may have requested films with greater penetration, which showed an area of decreased density in the liver; but it does not show in this film. Everything here indicates atelectasis and an elevated diaphragm, probably due to faulty respiratory effort.

DR. RICHARDSON: Usually when I come to this last stretch I know which horse I am going to bet on. Today I was going to make up my mind after seeing the x-ray films. I was thinking of two things. One was pulmonary infarct, but there was no history of cough with sputum and I was reluctant to accept that. The other possibility was coincidental carcinoma of the lung. From the appearance of the film and from Dr. Schulz's discussion I think that I shall leave the diagnosis as I originally stated it; I shall disregard this area of increased density and say that it was due to atelectasis. My diagnosis is chronic idiopathic ulcerative colitis with liver abscess.

DR. JONES: I am sorry that Dr. McKittrick is not here. This patient was very interesting. Dr. McKittrick and I felt that she had intrahepatic sepsis. As she was followed through her illness there was more and more compression tenderness over the liver, and some right subcostal tenderness. As a rule these signs when combined with a septic temperature are diagnostic of infection within the liver. The liver itself could be palpated even without compression and was quite tender. Before her death we were certain that she had abscess formation in the liver. Because of the succession of chills and fever I thought, and I believe Dr. McKittrick felt the same way, that there were multiple abscesses rather than a single one. Dr. Richardson mentioned the remote possibility of amebic abscess. As a rule a leukocytosis of this degree does not occur with amebic abscess; usually there is only a moderate leukocytosis. The fever can be extremely high in either amebic abscess or amebic hepatitis, but one usually does not get the combination of chills and fever and the intense leukocytosis that was present here.

There are one or two points I should like to add. In the first place there was no excuse for her developing such serious complications in her illness. This should represent a criticism of the medical treatment. The reason was that after

ileostomy she was reluctant to see a physician for any symptoms whatever and subsequently kept away from all physicians. Another point that is worth mentioning is the paucity of cases of ulcerative colitis that show intrahepatic disease. I have always thought that, with serious infection in the bowel draining eventually into the portal area, hepatic disease should develop more frequently. We have, however, seen only two or three cases associated with ulcerative colitis. It is the exception rather than the rule. When infection does occur it is usually localized in the pelvis or perianal region.

I was under the impression that there was one film that did show a probable cavity in the liver substance. On the basis of that and of the clinical picture, roentgenograms were taken after the administration of thorast to determine whether there was a single abscess or multiple ones.

DR. SCHULZ: We have the films here. The liver is riddled with multiple abscesses, which are in contrast to the liver substance where the thorast was taken up by the Kupffer cells.

CLINICAL DIAGNOSES

Multiple liver abscesses.
Ulcerative colitis.

DR. RICHARDSON'S DIAGNOSIS

Chronic idiopathic ulcerative colitis
Multiple liver abscesses.

ANATOMICAL DIAGNOSES

Ulcerative colitis, chronic.
Pylephlebitis, with liver abscesses, multiple
Pulmonary atelectasis.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy on this patient showed evidence of long-standing, ulcerative colitis with little if any activity. The bowel wall was markedly thickened, so-called "hose-like," with a very narrow lumen. The widest circumference of the bowel was 2.5 cm., about a quarter of the normal bowel circumference, and at one point it was 1.5 cm. with only a tiny lumen. This atrophy was obviously due to disuse. (In one case, which came to autopsy about ten years after ileostomy, the rectum and sigmoid were so atrophic that in places no lumen could be found.) The liver was adherent to the diaphragm on the right side, was extremely large, weighing 3500 gm., and contained multiple abscesses (Fig. 1). The main portal vein contained an infected thrombus, which extended into both radicles, more into the right than into the left. There was also free pus in the

portal veins. There were many large, greenish abscesses throughout the liver. It is quite obvious that surgical drainage of so many abscesses would have been impossible. We cultured the abscesses and the blood, but recovered only proteus bacilli. The spleen weighed 450 gm, and there was throm-

bos in the splenic vein. There were no chills, fever, night sweats or chest pain until "recently," when he had noted sharp twinges of pain in the right upper chest unassociated with cough or hemoptysis. There had been no history of inhalation of for-



FIGURE 1 Photograph of Cross Section of Liver Showing Multiple Abscesses and Portal Vein Thrombosis

bosis in the splenic vein. Although we examined many of the veins in the pericolic fat we were not able to find the actual source of the liver abscesses. Nevertheless, the hepatic infection was unquestionably secondary to the colitis.

The bone marrow showed a marked myeloid hyperplasia with replacement of the fat cells. We found nothing but atelectasis in the lung to account for the roentgen shadows in the right lower lobe. This is the only case of liver abscess associated with idiopathic ulcerative colitis that I can recall.

CASE 29462

PRESENTATION OF CASE

An eighteen-year-old boy was first seen in the Out Patient Department, about one year before the present admission, because of hemoptysis of four years' duration.

At the age of thirteen, while playing, he coughed up several large blood clots. He had a similar episode one week later, and these were repeated intermittently up to the day of his visit to the Out Patient Department. The amounts varied from a speck to half a cupful. No statement was made concerning the fre-

quency of the attacks, but "at no time were they more than two weeks apart." There were no chills, fever, night sweats or chest pain until "recently," when he had noted sharp twinges of pain in the right upper chest unassociated with cough or hemoptysis. There had been no history of inhalation of for-

eign body, antecedent upper respiratory infection, known contact with tuberculosis or undue bleeding tendency. He had fractured the left collar bone one year before onset of his symptoms, for which he was in a cast for two months. Examination in the Out Patient Department showed a well developed and well-nourished boy in no distress. The chest was well developed. There was dullness over the right upper lobe posteriorly to the midscapular region and anteriorly to the fourth rib, with occasional expiratory bubbling and coarse crepitant rales posteriorly. Kronig's isthmus was slightly narrowed on the right. The lungs were otherwise clear. The heart was in its usual position and normal in size. The abdomen was negative. There was no clubbing of the fingers.

The blood pressure was 138 systolic, 68 diastolic. The temperature was 98°F, the pulse 60, and the respirations 20.

X ray examination of the chest showed a round, homogeneous soft-tissue mass in the upper posterior mediastinum measuring approximately 11.5 cm. in diameter, without any evidence of calcification or cavity formation. The tumor obliterated the upper portion of the right bronchus. The visible portion of the right

appeared clear. The hilar shadows were normal and equal on both sides. The heart was not remarkable. No definite bone involvement could be seen, but there was a questionable pressure de-

cially at night. No other information was given regarding these attacks except that "he was quite free of wheezes at times." He was free of pain and maintained his weight. Bronchoscopy showed "ex-



FIGURE 1. *Chest Roentgenogram (Bucky) Showing Mass in the Right Upper Chest.*
The arrows point to the irregular area discussed in text.

fect on the right lateral aspect of the fourth dorsal vertebra, with narrowing of the right pedicle. The trachea appeared straight in the midline, and there was no mediastinal displacement. No fluid was present. Bucky films of the chest confirmed the presence of the large mass in the lung. An area of probable slight erosion of the upper aspect of the sixth rib was also seen. There was an irregular air pattern in the region of the mass, probably due to partially collapsed lung that was superimposed on the shadow of the mass (Fig. 1).

While being followed in the Out Patient Department, the patient developed wheezing, espe-

trinsic pressure but failed to reveal the source of the bleeding, although a moderate amount of bright-red blood was seen in the trachea and right main bronchus." Hospitalization was advised but refused.

For the next ten months he remained free from pain, hemoptysis and cough. At the end of the period he obtained a job in a weaving mill, doing heavy labor. Eight days before entry he suddenly became dyspneic while working. The dyspnea forced him to leave his work. Six days prior to admission he developed severe pain in the right anterior chest and he was admitted to a commu-

nity hospital, where x-ray films showed a lobulated tumor mass in the upper half of the right lung, with pleural effusion. Two chest taps yielded 100 and 300 cc. of reddish-brown pleural fluid and gave considerable relief. He was transferred to this hospital.

Physical examination showed a poorly nourished, cyanotic and dyspneic man with anxious, pale facies and visible flaring of the alae nasi on breathing. The right chest was splinted during inspiration. There were dullness and diminished tactile fremitus and breath sounds over the right upper and lower lobes. Dullness was obtained over the right middle lobe, with egophony and increased tactile fremitus. Pectoriloquy was heard over the right upper lobe posteriorly and over the middle lobe anteriorly. The diaphragmatic excursion was poor on the right. The heart was normal. The remainder of the examination was not remarkable.

The blood pressure was 130 systolic, 60 diastolic. The temperature was 99.6°F., the pulse 128, and the respirations 25.

Examination of the blood showed a red-cell count of 4,100,000, with 75 per cent hemoglobin. The white-cell count was 11,000 with 89 per cent neutrophils. A blood Hinton test was negative. The prothrombin time was 28 seconds (normal, 16 seconds); the hematocrit was 39.2 per cent. The nonprotein nitrogen was 10 mg. per 100 cc., and the protein 5 gm. The van den Bergh test was normal. Urinalysis was negative.

X-ray examination of the chest, almost a year after the first one, showed the tumor mass still present. The right pleural cavity was filled with a fairly large amount of fluid and there was partial collapse of the right middle and lower lobes, which had a honeycombed appearance. The left lung appeared clear, but there was questionable crowding of the markings in the left lower lobe.

During the next ten days, three chest taps yielded 2800, 1500 and 1000 cc. of dark, bloody fluid, which on smear and culture was negative for organisms. No tumor cells were seen in the sediment.

Repeated x-ray studies after the taps showed that, instead of a fluid level, there was an area of increased density with irregular markings extending along the lateral axillary line. There were numerous irregular areas of decreased density in the right upper chest, either in the tumor or in the pleural cavity. None of the visualized bones, especially the ribs, showed evidence of destruction, and no other changes were noted. Another bronchography, a year after the first, was negative. No evidence of intrinsic or extrinsic tumor was seen.

On the eleventh hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. AUSTIN BRUES: I should like to discuss this case mainly from the standpoint of its natural history, which seems rather specific and characteristic. The boy had a lesion that had apparently existed for at least five years and first gave symptoms at the age of thirteen. The history divides itself into three phases. First, there was a long period in which the only symptom was rather persistent hemoptysis. Secondly, after four or more years there was a period of wheezing, suggesting bronchial compression. Finally, there was an acute sudden episode with pain in the anterior chest and dyspnea, and the rapid development of bloody pleural effusion. To this history we can add the finding of a round mass inside the chest, apparently arising from the posterior mediastinum, and presumably the seat of the symptoms. We have no evidence of disease elsewhere in the body, except that he had a prolonged prothrombin time and a low serum protein. However, the van den Bergh test was normal, and we have insufficient evidence to implicate the liver.

The question that we have to settle is, What sort of isolated mass in this location will progress to give this sort of history? Obviously this was not an acute infectious process. It might conceivably have been due to tuberculosis of the bronchial nodes or to tuberculosis arising from the spine. The entire early course of the process, however, was essentially silent except for hemoptysis, and there was no evidence of infection or tuberculosis elsewhere. I consider that an infectious process of any sort is unlikely. A hydatid cyst of the mediastinum, first giving rupture into the bronchus, later into the pleural cavity, might give rise to this sequence of symptoms; but we have no reason to suspect an unusual environmental association and the patient had no eosinophilia. Moreover, no eosinophilia was noted even after extension of the process into the pleural cavity, which, if due to rupture of a hydatid cyst, would have caused a certain amount of the cyst contents to be absorbed.

In a young patient we must think of a congenital anomaly—bronchostenosis or a lung cyst. A condition of this sort would most likely progress to serious symptoms only if it became secondarily infected. Again I point out that infection was not a perceptible element in the clinical picture.

This brings me to tumor. The long duration is in favor of a benign tumor or a tumor that underwent malignant change late, that is, during the last year. Lymphoma can exist for a period of

many years without characteristic progression. Such a lymphoma would be the giant follicular type or a very scirrhous type of Hodgkin's disease. I should point out that hemoptysis is a rare symptom in lymphoma, and if it does occur it suggests that one is dealing with a particularly invasive form, which would not be the type giving a long, relatively quiescent history. It seems to me the presumptive diagnosis is a teratoma, not well enough differentiated, as is the classic dermoid cyst, to show calcification by x-ray or to yield hairs or other recognizable elements in the sputum or pleural fluid. The life history of this process is emphatically in favor of this diagnosis. These tumors appear early in life, may give their first symptoms at puberty or later, and sometimes give hemoptysis over a long period. Eventually they are likely to undergo malignant change or to rupture. I should be in favor of rupture as the explanation of the final episode here because of the extreme acuteness of its onset, although invasion of the pleura is a possible explanation, and would point to malignant change. I do not believe that it is necessary to assume, however, that the process had become malignant.

The fly in the ointment is the location of the lesion. It was apparently posterior in position, whereas dermoid cysts and teratoid tumors are almost always found in the anterior mediastinum.

Typical neoplasms of the posterior mediastinum are of neural origin. The history, however, is against one of these. They grow behind the pleura, and one would not expect cough and hemoptysis to be the earliest symptoms. Because of their location they frequently produce Horner's syndrome or pain early in the course of their development. The first symptom here was hemoptysis, which suggests that the lesion was near the bronchi and not posterior to the pleura. There are various rare tumors, such as chondroma, endothelioma, angioma and lipoma, that might arise in this location. There is one thing somewhat in favor of the possibility of an angiomatous tumor—the characteristic picture of bleeding with which the history started.

I wonder if we might see the x-ray films.

DR. LAURENCE L. ROBBINS: These films show a fairly smooth mass arising posteriorly in the mediastinum, or apparently arising in the mediastinum. The one thing in favor of the neural type of tumor, in addition to its location posteriorly, is that there is a definite erosion of the pedicle of the fourth thoracic vertebra. So far as the ribs are concerned, I am not at all sure that there are any definite changes. This is the shadow described as an irregular area overlying the mass and representing aerated lung (Fig. 1). I am not

convinced of that. The only other possibility is that it is fat within the tumor. It is difficult to be sure, and most likely it is air in the overlying lung.

These are the films taken at the time of the second admission; they show a large amount of fluid in the pleural cavity and disease in the right lower lobe. The mass and the shadow, which is either air or fat, are still present. This view, with the patient on his side, was taken after a tap to determine whether there were pleural metastases. There are irregularities along the pleura, but they are most likely masses of fibrin rather than metastases, because fibrin is usually present with bloody fluid. One cannot, however, positively rule out metastases.

DR. BRUES: I am going to let my diagnosis rest on the history rather than on the location and to assume that the tumor arose near the bronchi rather than posterior to the pleura. I shall say that it was a teratoid tumor.

DR. RICHARD H. SWEET: Might I say as a representative of the service that saw the man before he was operated on that we did not believe, at least I did not believe, that he had a benign tumor. In fact I have never seen a benign mediastinal tumor produce bloody effusion. My personal diagnosis was, and I suspect some of the others who saw the patient were of the same opinion, a malignant tumor, probably teratoma. Dr. Brown operated on this patient. What does he say?

DR. ROBERT K. BROWN: We did a thoracoscopy and did not see much except a large empty space with implants of fibrin on the chest wall. Biopsies were taken of these and they were not malignant. Since we still thought that the tumor was malignant, the patient was explored. The preoperative diagnosis was malignant neurogenic tumor or neurofibrosarcoma, because we thought that it arose in the posterior mediastinum.

At operation there was a large cystic mass in the upper part of the right thorax. This contained a hole, and the rupture was probably the cause of the bloody pleural fluid. A biopsy specimen was taken from the wall of the cystic mass at the edge of the rupture, and on cutting, it was evident that there was lung tissue adherent to the wall of the mass. I thought this was collapsed lung plastered over the cyst. The patient died following operation.

DR. BENJAMIN CASTLEMAN: Would anyone want to venture a diagnosis at this point?

DR. RALPH ADAMS: I have no idea what was wrong with this man. I think that the lesion arose in his lung because of two factors that almost have to place it in the lung. First, there was frequently recurring hemoptysis. There was

a rule here a few years ago that daily hemoptysis meant carcinoma. After three years we found an exception in a case of bronchiectasis. That was the first exception, and I have since encountered one other. In the second place, this man had a wheeze, indicative of developing bronchial obstruction. My personal diagnosis, if I were about to operate, would be slowly growing sarcoma of the lung. I believe that sarcoma in the lung has occurred in this hospital only once.

DR. SWEET: That is correct.

DR. ROBBINS: How do you explain the erosion of the pedicle of the fourth thoracic vertebra if it is a primary lung tumor?

DR. ADAMS: I could not explain it as a primary lung tumor unless it were sarcoma of the lung. If it were a sarcoma arising in the mediastinum and invading the lung the explanation would be easy.

DR. GEORGE W. HOLMES: Is there anything to show why there was such a delay between the first roentgenologic examination and operation?

DR. CASTLEMAN: The patient refused operation.

CLINICAL DIAGNOSIS

Superior mediastinal tumor, with rupture into the pleural cavity.

DR. BRUES'S DIAGNOSIS

Teratoid tumor of mediastinum, with rupture into the pleural cavity.

ANATOMICAL DIAGNOSIS

Neurofibroma of lung, with cystic degeneration and rupture into the pleural cavity.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The material that Dr. Brown removed from the cyst or tumor was composed

of spindle-shaped cells, some in whorls, which strongly suggested a neurogenic benign tumor. In favor of this was the presence of huge numbers of so-called "foam cells," that is, large lipid-laden mononuclear cells. That is probably the reason why Dr. Robbins thought he saw fat in the tumor. Certainly a large part of the tumor was composed of cells filled with fat. Lipoid degeneration of a neurofibroma is not at all uncommon. We were fairly certain that the tumor was benign.

The autopsy specimen shows that this tumor was within the lung. It had broken down so much that it had become cystic. This cystic mass, which was about 7 or 8 cm. in diameter, communicated with the apical branch of the right upper lobe bronchus, and this certainly accounted for the long-standing hemoptysis. I believe that the tumor probably arose close to the bronchus, or perhaps in it, and degenerated slowly as it gradually increased in size. There was lung tissue surrounding the cyst on all sides except over the area where it had ruptured.

We have had 2 other cases of neurofibroma of the lung. One was in a man of thirty who had all the signs and symptoms of a bronchial adenoma, that is, bronchial obstruction with hemoptysis. Bronchoscopic biopsy showed it to be a neurofibroma, and Dr. Benedict removed the tumor via the bronchoscope in three operations.

DR. EDWARD B. BENEDICT: The patient was completely relieved by bronchoscopy. I have not seen him for three years. He had no apparent lung damage.

DR. CASTLEMAN: The other case was one in which Dr. Churchill performed a lobectomy for a well-circumscribed tumor that pressed on a bronchus but had not actually invaded its mucosa.

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UNITED WAR FUND

No one knows better than physicians the valuable contribution to community life made by the two hundred and sixty-four hospitals, dispensaries, clinics and other health and social services that share in the Greater Boston Community Fund. Possibly no group of citizens gives more of itself to the 400,000 persons who depend on these agencies to help adjust themselves to life's problems. In either case, or perhaps because of both, physicians of Greater Boston are bound to be generous to the appeal now being made for these community services. But that's not all. The \$7,500,000 goes two ways. Whereas approximately \$5,500,000 is al-

located to Community Fund needs, \$2,000,000 goes directly to such war-related services as the USO, War Prisoners Aid, United Seamen's Service and relief of the stricken peoples of the Allies.

The physician must think twice when the solicitor asks for his gift this year. He will want, first of all, to do something for that bright-eyed little youngster whose parents have deserted him. Then, of course, he must help the USO, which is doing such a magnificent job everywhere, and he cannot resist the appeal to make a token gift for all the brave people overseas who are suffering unknown hardships in this war, while he and his family live safely and snugly at home. GIVE — BECAUSE YOU CAN.

SO LITTLE TIME

THE majority of us are so constantly confronted with the perplexing problem of fitting our commitments into an allotted daily twenty-four hours that we view with amazement and despair the activities of individuals like, let us say, Prime Minister Churchill. Writer of history and maker of history, he has found time in his abundant life to fight in one war and direct another, to make books and speeches, to lay bricks, to paint pictures and to save an empire.

John Buchan, later Lord Tweedsmuir, was a writer of note before he became a statesman and finally governor general of Canada; we are familiar with the dual activities of Disraeli, romantic novelist and statesman without peer, who presented Queen Victoria with the empire that Churchill has kept intact; Bulwer-Lytton was a novelist and statesman, if not pre-eminent as either; General Lew Wallace wrote one of our really outstanding historical novels; and General Patton, we are told, is a poet of no little merit! These men, whether satisfied with their achievements or not, have at least found time to make some contributions to the world in which they found themselves.

It is a common experience of those who are sensitive to life, who feel the need of some personal

fulfillment, some satisfying justification for their existence, to awaken rather late, and suddenly, to a realization of life's self limitation. The allotted years are never really enough, nor does anyone know the sum and extent of his allotment. We accumulate, as we go, a squirrel cage full of little duties and activities that may keep us moderately comfortable because of a real communion with our selves, but we seldom find time to realize the dreams of youth or to search out the various talents that may lie in each one of us. We use our work and our play, our recreations and our amusements, as anodynes to keep us from a full realization of our relative futility.

Some stern moral censor devised a comfortless motto for sundials. What could possibly be more effective than the ominous epigram, "It is later than you think," to destroy the pleasure of a sunny hour in a garden? John Marquand must have been deciphering this legend just before he developed the theme of middle aged frustration in his newest book, *So Little Time*. Middle age is a bit late to realize how little time there is, but it is the period of life in which we usually appreciate it—except, perhaps, for those happy extroverts who never realize it at all.

Time is an elusive commodity, and the greatest gift that man can have or develop is the ability to use it intelligently, if not industriously. Every individual is given the same amount of time in each twenty four hours—which sounds like a truism, but is really a fundamental and dimly appreciated truth. The only difference in this respect is that some of us are given more units to use than are others. Next in importance is a sense of values that will help us to see clearly those of our own qualities that can be developed and the wishes that can reasonably be fulfilled. If we wish to avoid frustrations, we must choose the goal that is within our reach, we must work steadily toward it, and we must start early enough. The only qualification that need apply to this goal is that it must satisfy the person who is seeking it.

MEDICAL EPONYM

KUMMELL'S DISEASE

Professor Hermann Kummell (1852-1937) described this condition in a paper, entitled "Die rarefiierende Ostitis der Wirbelkörper [Rarefactive Ostitis of the Vertebral Bodies]," published in the *Verhandlungen der Gesellschaft deutscher Naturforscher und Aerzte* (64: 282-285, 1892). A portion of the translation follows:

To sum up, we are dealing with an injury, often of trifling nature, that affects the vertebral column either directly or indirectly, and so far as the immediate effect is concerned leaves no sign of its occurrence. After months of complete health, there begins a rarefactive process in the vertebrae which finally results in atrophy of their substance. Suppuration does not occur in this pathologic process as in tuberculous spondylitis, nor is there any thickening of the bony mass, as in syphilitic processes, or bony deposition and change, as in arthritis deformans.

The diagnosis of the condition, after what has been said, offers no great difficulties and if we consider the most important factors—the effect of trauma in an otherwise healthy person, transitory pains and gibbus formation later, with the accompanying local and referred discomfort—confusion with tuberculous spondylitis or other disease of the vertebrae is easily avoided.

R W B

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

CUSHMAN—HOWARD L. CUSHMAN, MD of Methuen died November 4. He was in his fifty-eighth year.

Dr Cushman received his degree from Boston University School of Medicine in 1908. Up to the time of his death he served as school physician in Methuen. He was a member of the Massachusetts Medical Society, the American Medical Association, the Lawrence Medical Association and the Lawrence Medical Club.

His widow and a brother survive.

DAVID—ERNEST J. DAVID, MD of Lowell died July 11. He was in his sixtieth year.

Dr David received his degree from Laval University Faculty of Medicine, Quebec, in 1915. He was a member of the Massachusetts Medical Society and the American Medical Association.

HALLORAN—ROY D. HALLORAN, MD of Waltham died November 10. He was in his fiftieth year.

Dr Halloran received his degree from Columbia University College of Physicians and Surgeons, New York, in 1920. He served as an intern at the Newark (New Jersey) City Hospital from 1920 to 1922 and later as assistant physician at the New Hampshire State Hospital in Concord. He joined the staff of the Boston State Hospital in 1922 and served as assistant superintendent in 1928 and 1929. In 1925 he and Dr Abraham Myerson of Boston founded the hospital's research department. In

1933 Dr. Halloran was named the first superintendent of the Metropolitan State Hospital, a post that he held until he took leave of absence in July, 1942, to be commissioned a colonel in the Army Medical Corps. His job in the Army was to organize and co-ordinate the neuropsychiatric service in all Army branches, at home and overseas. He was a member of the American Psychiatric Association, New England Society of Psychiatry, Massachusetts Medical Society and American Medical Association, as well as professor of clinical psychiatry at Tufts College Medical School.

His widow, a daughter and a son survive.

KENNISON—**FREDERICK M. KENNISON, M.D.**, of Boston, died July 31. He was in his eighty-first year.

Dr. Kennison received his degree from Tufts College Medical School in 1905. He was a member of the Massachusetts Medical Society and the American Medical Association.

MILLER—**HOWARD S. MILLER, M.D.**, of Taunton, died September 6. He was in his fifty-sixth year.

Dr. Miller received his degree from Middlesex University School of Medicine, Waltham, in 1922. He was a member of the Massachusetts Medical Society and the American Medical Association.

THOMPSON—**CLARA L. THOMPSON, M.D.**, of Boston, died September 16. She was in her seventy-third year.

Dr. Thompson received her degree from the College of Physicians and Surgeons, Boston, in 1915. She was a member of the Massachusetts Medical Society and the American Medical Association.

WASHBURN—**FRANK H. WASHBURN, M.D.**, of Holden, died November 10. He was in his seventy-third year.

Dr. Washburn received his degree from Tufts College Medical School in 1899. Dean of physicians in Holden, he was a founder and chief surgeon at the district hospital and a fellow of the American College of Surgeons. He was consulting surgeon at the state sanatorium and the United States Veterans Hospital, both in Rutland Heights. He was a councilor of the Massachusetts Medical Society, past president of the Worcester District Medical Society, a member of the American Medical Association, American Urological Association, New England Urological Society, Trudeau Society, American Society of Regional Anaesthesia and the New England Roentgen Ray Society.

His widow, a daughter and two sons survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

GONOCOCCUS CULTURE SERVICE

The Massachusetts Department of Public Health announces a new service to physicians of Massachusetts. The superiority of cultural methods over smear methods in detecting gonococci in certain types of gonococcal infections is now well recognized, and the department is of the opinion that

utilization of cultural methods will be of aid in the control of such infections.

Mailing of specimens. Recent advances in methods of sending specimens through the mail for cultural studies indicate that such delayed cultures are less efficient than cultures planted immediately after obtaining the specimens, but considerably more efficient than the examination of stained smears. Any physician wishing to utilize this service should request mailing kits from the Bacteriological Laboratory, Room 527, State House, Boston. Instructions for obtaining specimens will accompany each mailing outfit.

Storage of mailing outfits. The fluid in which the specimens are placed for mailing will maintain its efficiency only if kept in the icebox, and for a period not to exceed six weeks. All containers will be stamped with an expiration date, and if not used by that time they should be returned to the laboratory, whereupon fresh outfits will be sent to the physician on request. It should be emphasized that mailing outfits kept at room temperature before being inoculated do not give satisfactory results.

Relative value of cultures. Cultures are but slightly more efficient than smears in detecting gonococci in male patients who have a purulent urethral discharge, but far more efficient than smears in detecting gonococci in prostatic secretions as a test of cure. Cultures are more efficient than smears in detecting gonococci in both adult and immature females in all stages of gonococcal infection.

Precautions to ensure satisfactory specimens. The efficiency of the cultural method depends greatly on the physician's care and expertness in obtaining satisfactory specimens. The instructions on the card in the outfit are brief but if followed in detail should ensure satisfactory specimens.

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR OCTOBER, 1943

RÉSUMÉ

DISEASES	OCTOBER 1943	OCTOBER 1942	SEVEN-YEAR MEDIAN
Anterior poliomyelitis ..	57	5	11
Chicken pox ..	485	291	333
Diphtheria ..	18	11	15
Dog bite ..	721	812	612
Dysentery, bacillary ..	24	314	21
German measles ..	82	57	35
Gonorrhea ..	435	384	416
Measles ..	402	541	291
Meningitis, meningococcal ..	45	11	6
Meningitis, other forms ..	13	3	•
Meningitis, undetermined ..	11	0	•
Mumps ..	158	401	204
Pneumonia, lobar ..	161	242	227
Salmonella infections ..	14	13	3
Scarlet fever ..	624	621	362
Syphilis ..	380	610	450
Tuberculosis, pulmonary ..	259	236	238
Tuberculosis, other forms ..	16	11	29
Typhoid fever ..	4	7	7
Undulant fever ..	6	6	5
Whooping cough ..	322	731	555

*Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

COMMENTS

The month of October has produced a long list of diseases more or less above the seven-year median. Anterior poliomyelitis is still at a point five times that of the seven-year median, but, on the other hand, the current

month's figure is less than half that of last month. Apparently the summer's outbreak is well on the wane.

Scarlet fever, which has been at an unusually high level all this year, seems to have begun again the usual seasonal upswing following the summer drop.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Amherst, 1; Arlington, 1; Attleboro, 3; Beverly, 7; Boston, 2; Cambridge, 2; Danvers, 3; Fall River, 6; Fitchburg, 1; Hamilton, 1; Hopedale, 1; Ipswich, 1; Lee, 1; Lowell, 2; Lynn, 2; Medford, 3; Methuen, 1; Natick, 3; New Bedford, 2; North Attleboro, 1; North Reading, 1; Norwood, 1; Plymouth, 1; Quincy, 1; Saugus, 1; Seekonk, 1; Swansea, 2; Topsfield, 1; Waltham, 2; Walpole, 1; Watertown, 1; Weymouth, 1; total, 57.

Anthrax was reported from: Haverhill, 1; total, 1.

Diphtheria was reported from: Boston, 6; Bourne, 1; Chicopee, 1; Lowell, 3; Medford, 1; New Bedford, 2; Salem, 2; Somerville, 1; Taunton, 1; total, 18.

Dysentery, bacillary, was reported from: Beverly, 2; Boston, 3; Brockton, 1; Brookfield, 1; Cambridge, 1; Easthampton, 1; Malden, 11; Northampton, 1; Wellesley, 3; total, 24.

Encephalitis, infectious, was reported from: Worcester, 1; total, 1.

Malaria was reported from: Amherst, 2; Brookline, 1; Fort Banks, 11; Fort Devens, 2; total, 16.

Meningitis, meningococcal, was reported from: Arlington, 1; Beverly, 1; Boston, 12; Brookline, 1; Cambridge, 1; Chelsea, 2; Chelsea Naval Hospital, 3; Fall River, 1; Fort Devens, 2; Framingham, 1; Lowell, 1; Needham, 1; New Bedford, 1; Newburyport, 1; Newton, 1; North Brookfield, 1; Plymouth, 1; Salem, 1; Scituate, 1; Somerville, 1; Southbridge, 1; Waltham, 2; Wellesley, 1; Weymouth, 1; Winthrop, 1; Worcester, 4; total, 45.

Meningitis, other forms, was reported from: Boston, 3; Cambridge, 1; Haverhill, 1; Ipswich, 1; Marblehead, 1; Medford, 1; Methuen, 1; Northbridge, 1; Salem, 1; Springfield, 1; Waltham, 1; total, 13.

Meningitis, undetermined, was reported from: Boston, 4; Milton, 1; Palmer, 1; Quincy, 2; Springfield, 1; Worcester, 2; total, 11.

Salmonella infections were reported from: Boston, 1; Bridgewater, 1; Cambridge, 1; Chelsea, 1; Chicopee, 2; Leominster, 1; Lowell, 1; Lynn, 2; Medford, 1; Westboro, 1; Weymouth, 1; Worcester, 1; total, 14.

Septic sore throat was reported from: Boston, 6; Brockton, 1; Malden, 1; Natick, 1; Swampscott, 1; total, 10.

Tetanus was reported from: Springfield, 1; total, 1.

Trachoma was reported from: Medford, 1; total, 1.

Tularemia was reported from: Falmouth, 1; total, 1.

Typhoid fever was reported from: Brookfield, 1; Dartmouth, 1; Medford, 1; New Bedford, 1; total, 4.

Typhus fever was reported from: Chelsea, 1; total, 1.

Undulant fever was reported from: Adams, 1; Franklin, 1; Methuen, 1; Southbridge, 1; Southwick, 2; total, 6.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Haverhill	December 1	William T. Green
Lowell	December 3	Albert H. Brewster
Salem	December 6	Paul W. Hugenberger

Brockton	December 9	George W. Van Gorder
Springfield	December 15	Garry deN. Hough, Jr.
Worcester	December 17	John W. O'Meara
Pittsfield	December 20	Frank A. Slowick
Fall River	December 27	Eugene A. McCarthy
Hyannis	December 28	Paul L. Norton

WAR ACTIVITIES

CIVILIAN DEFENSE

MANUAL ON EMERGENCY CARE OF INJURED

The immediate care that can be given to injured persons at the site of a disaster and the technics of transporting them to safety and medical attention are described in a new manual issued by the Medical Division, Office of Civilian Defense. The work is based on procedures and organization developed by the OCD and on careful study of three years of British and other air-raid experience. The 117-page book is divided into three parts: "Civilian Defense," "Emergency Field Care," and "Transportation of the Injured."

Part I describes the organization and operation of the field casualty service developed by the Medical Division, which includes mobile medical teams, based on hospitals wherever possible; express parties, made up of a medical team, a rescue squad, an ambulance, and a car for sitting cases, dispatched through the control center to a disaster for immediate action; casualty stations for the care of casualties with minor injuries; stretcher teams; and ambulances.

Part II includes a discussion of the injuries and conditions most frequently encountered in wartime disasters—namely, hemorrhage, shock, fractures, burns, suffocation and carbon monoxide poisoning. There are chapters on principles of bandaging, with detailed illustrations; marking of casualties and disposal of the dead; methods of blanketing a casualty; and methods of lashing a casualty to a stretcher.

Special attention is given to crush and blast injuries. Crushing wounds may result from falling masonry, girders, beams or whole floors dislodged by bomb explosions. Although these injuries may be immediately fatal, casualties often show little sign of injury when released, the manual points out. Their condition may appear good for a few hours and yet they may die of kidney failure several days later. Directions for first aid are included, and workers are warned that any person who has been trapped by debris which has pressed on any part of the body must be regarded as a serious casualty. The importance of administering by mouth abundant quantities of fluids and alkalis (sodium bicarbonate) is stressed. Persons exposed to blast from high explosives may also suffer serious internal injury without external evidence of it. The manual urges all persons concerned with the handling of casualties to suspect blast injuries in every person found near the site of a bomb explosion, especially those who have obviously suffered injury and yet show no external evidence of it. More extensive discussions of these two types of injury are included in the recent OCD publication, *Clinical Recognition and Treatment of Shock*.

Part III, devoted to transportation of the injured, describes regular and improvised stretchers and gives directions for stretcher bearing, with a separate section on types of injury that require special care in moving. Another chapter explains methods of carrying the injured without stretchers, and the final chapter explains the ambulance

service of the civilian-defense organization and presents specific instructions for loading and unloading ambulances. The latter instructions describe procedures required if war gases are encountered.

The manual is intended primarily for the training of rescue workers, medical auxiliaries, ambulance drivers and attendants, and stretcher bearers of the Emergency Medical Service. In the appendix are a schedule of training based on the manual; the OCD operations letters describing the work of stretcher teams, the Rescue Service and instructions on self-aid in case of exposure to war gas; and a section on electrical hazards.

MISCELLANY

GRANT TO PROMOTE MEDICAL INFORMATION

Dr. Ross G. Harrison, chairman of the National Research Council, has announced the acceptance by the Council of a grant from the Johnson and Johnson Research Foundation in the amount of \$75,000. The grant was made to enable the Division of Medical Sciences, under the chairmanship of Dr. Lewis H. Weed, to gather medical information pertaining to the war effort and to disseminate summaries. The program of the Division of Medical Sciences of the National Research Council contemplates coverage of the various medical reports and bulletins that emanate from civilian and military activities throughout the world. The enterprise should fill a much needed gap in the war effort in medicine, since one of the greatest difficulties encountered in medicine today lies in providing adequate up-to-date information to the medical officers of the armed services, both in this country and abroad, and in making the experience of war medicine available, so far as possible, to civilian physicians.

The Johnson and Johnson Research Foundation appropriation to the National Research Council becomes immediately available; in accordance with present plans it will be utilized in the period up to June 30, 1945. A central office will be established in Washington and reporters will be appointed in various foreign countries, so that a staff of special observers abroad will be working under the direction of the central office. The various theaters of operation present medical problems in which climate, season of year, distribution of insects and distribution of disease, all play different roles. Reports from widely separated parts of the world will be of the greatest medical importance and it is hoped that with the combined effort much of significance will be achieved.

AMA MEETING IN 1944

The Board of Trustees have recently announced that the 1944 annual session of the American Medical Association will be held in Chicago, June 12 to 16. The scheduled meeting place, St. Louis, had to be given up, owing to lack of adequate accommodations. The meetings of the House of Delegates will be held at the Palmer House, which will also house the Scientific Exhibit. The Technical Exposition will be installed at the Stevens Hotel.

The Scientific Exhibit will cover all phases of medicine and the medical sciences with particular emphasis on graduate medical instruction for the physician in

general practice. Application blanks for space in the exhibit are now available and may be obtained by communicating with the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago 10.

BOOK REVIEWS

Air-Borne Infection: Some observations on its decline. By Dwight O'Hara, M.D. 8°, cloth, 114 pp., with 11 charts. New York: The Commonwealth Fund, 1943. \$150.

The author challengingly but plausibly includes in this series of essays on air-borne infection not only a consideration of the scope of preventive medicine but also chapters on smallpox, streptococcal infections, rheumatic fever and the aging process, in addition to his discussion of upper respiratory infections and tuberculosis. He suggests that preventive medicine has enjoyed over the years the company of a silent partner, and attempts to analyze the spontaneous or indirect factors that have influenced the results of man's conscious effort at control of infection. Health—the physiologic integrity of the tissues—must not be confused with the mere control of conditions prejudicial to health.

This book will wear well because it thoughtfully interprets some rather striking factual data. The contributions of some investigators rust out because their squeaking metallic facts are not sufficiently oiled with interpretive thought. This little volume is well lubricated. It is also well written, and in this respect, as well as in thought and content, it follows in the tradition of such contributions as that of Bigelow on self-limited diseases. It will be read with pleasure and profit by all who are concerned with the problem of keeping men alive and well.

Biochemistry and Morphogenesis. By Joseph Needham. F.R.S. 4°, cloth, 787 pp., with 328 illustrations. Cambridge, England: University Press, 1942. \$1250.

No laboratory should be without this most important work, which deals with one of the fundamental problems of biology by a distinguished investigator. The purpose of the author is to show that the disciplines of chemistry and morphology are closely related. This object is achieved by bringing together the experimental evidence that shows that levels of organization are not alone anatomical but molecular, colloidal, paracrystalline, protein structural and fibrous macromolecular. All these orders are the natural consequence of the properties of matter.

The present study considers the chemical changes that go on during embryonic development. In 1931 the first successful embryonic inductions were obtained; this opened the way to the biochemical investigation of morphogenetic hormones. These substances are discussed in Part 1 under the heading of "The Morphogenetic Substratum," Part 2 deals with "The Morphogenetic Stimuli," that is, the isolation of the inductor substances. Part 3 discusses "The Morphogenetic Mechanisms."

There is a valuable glossary of 8 pages, and an excellent bibliography covers 70 pages. In addition there is a general index, as well as an index of animals, plants and genes. Every student of biology will find this book invaluable.

(Notices on page xii)

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BLOOD-PRESSURE DETERMINATIONS IN PATIENTS WITH ESSENTIAL HYPERTENSION*

III. Evaluation of Sympathectomy over a Three-Year to Five-Year Period

DAVID AYMAN, M.D.,† AND ARCHIE D. GOLDSHINE, M.D.‡

BOSTON

THE treatment of essential hypertension is far from established. The hope of successful therapy by renal extract has not materialized. Sympathectomy by one method or another has been performed in the past eighteen years in about 3000 cases, and the reports of results are also becoming numerous. The literature, however, indicates widely varying opinions concerning the effect of the different operations on the levels of blood pressure and the course of the disease. The present paper reports some preoperative and postoperative observations made during the past six years in an unusually controlled group of patients with essential hypertension. The observations of blood pressure were made not only by the usual clinic methods, but in addition by readings taken at the start of, during and after twenty-minute clinic rest periods¹ and the determination of the blood-pressure levels, made at home by the patients themselves both before and after operations.² In some cases, the data have been obtained continuously over periods as long as five years.

LITERATURE

Sympathectomy as a therapeutic measure for hypertension was apparently first suggested by Daniélopou³ in 1923. The first operation seems to have been done by Rowntree and Adson⁴ in 1925. The second, third and fourth lumbar ganglions were removed without significant effect in a patient with malignant hypertension. In 1927, Pieri⁵ described his technic of splanchnicectomy for hypertension, but did not mention his results.

These initial efforts have undergone much elaboration and modification. The first change was by Adson⁶ himself, who cut the sympathetic nerves by resection of the anterior root.⁶ This operation, requiring laminectomy, was apparently effective but has been given up because of its difficulty and high mortality. In 1934, Craig and Brown⁷ carried out unilateral and bilateral infradiaphragmatic splanchnicectomy, in a few cases with resection of the first and second lumbar ganglions. In 1935, Peet⁸ reported his initial studies of supra diaphragmatic bilateral splanchnicectomy. In 1937, Allen and Adson⁹ described subdiaphragmatic splanchnicectomy with lumbar ganglionectomy. adding, in some cases, partial adrenalectomy. In 1938, we¹⁰ had a case subjected to a seven-stage, almost total, bilateral sympathectomy. In 1940, Smithwick¹¹ combining the Pieri-Peet and Allen-Adson methods, described a two-stage bilateral transdiaphragmatic operation by which he removes the entire great splanchnic nerves, their aortic branches and the sympathetic ganglions—the ninth, tenth, eleventh and twelfth dorsal ganglions, the first lumbar and occasionally the second lumbar ganglion. Finally, Grimson¹² has reported a group of almost total, bilaterally sympathectomized cases.

The results in these and many other studies are widely divergent; they are not analyzed here.

METHODS USED IN THIS STUDY

Most therapeutic studies of hypertension are seriously marred by unscientific methods of control: the studies of surgical therapy thus far reported are no exception. In a previous paper, one of us (D. A.) indicated pitfalls to be avoided and outlined suggestions for proper controls in evaluating such therapy. The present paper is a report of findings made by these methods, includ-

*Presented at the annual meeting of the Massachusetts Medical Society, Boston May 26, 1943.

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TABLE 1. Preoperative and Postoperative Findings in 13 Patients with Essential Hypertension Subjected to Sympathectomy.

CASE No.	AGE	SEX	BLOOD-PRESSURE OBSERVATIONS						
			DURATION OF HYPERTENSION	PREOPERATIVE			POSTOPERATIVE		
				Duration of Clinic Visits with 20-Min. Rest Periods	No. of Clinic Visits with 20-Min. Rest Periods	Duration of Home Blood-Pressure Studies	Duration of Clinic Visits with 20-Min. Rest Periods	No. of Clinic Visits with 20 Min. Rest Periods	Duration of Home Blood-Pressure Studies
1	49	M	10	0	0	0	12	31	0
2	45	M	9	13	17	0	48	89	48
3	38	M	2	3	12	1			
4	35	F	15	7	19	3	51	29	51
5	42	F	4	6	8	0	60	12	1
6	24	M	1/12	0	0	0	7	7	0
7	41	M	1	1	4	1	54	41	30
8	33	F	2	1½	6	1½	154	15	54
9	33	F	8/12	7	10	6	57	12	57
10	37	F	8	3	10	2½	56	44	56
11	44	F	8	10	10	2½	54	45	54
12	48	F	6	12	18	4	39	39	39
13	33	F	4	0	0	7	18	7	½

CASE No	OCULAR FUNDI (KEITH-WAGENER)	HEART SIZE		ELECTRO-CARDIO-GRAM		INTRA-VENOUS PYELOGRAM	ALBUMIN-URIA	RENAL FUNCTION	LOWEST BLOOD PRESSURE AFTER SODIUM AMYTAL TEST	SYMPTOMS												
		PREOP	POSTOP	PREOP	POSTOP					PREOP.	POSTOP											
												Grade										
												mm./Hg.										
1	4	N	N	+	+	N	C	N	150 84	+	±											
2	3	N	N	+	±	N	0	N	-	+	++											
3	4	N	N	+	+	N	C	N	220 138	+	0											
4	3	N	N	N	N	N	0	N	-	+	±											
5	2	+	+	+	N	N	1	N	-	+	±											
6	4	+	+	+	+	N	C	+	138 98	+	±											
7	3	N	±	+	+	N	1	N	96 66	0	0											
8	2	N	N	N	-	N	C	N	146 100	+	0											
9	2	N	N	N	N	N	0	N	-	+	±											
10	3	N	N	+	N	N	0	N	120 80	+	0											
11	3	+	N	N	N	+	0	N		+	0											
12	3	+	±	+	±	N	1	N		+	0											
13	2	N	-	N	-	N	0	N	114 80	+	0											

C = constant; N = normal; + = enlarged, abnormal or present; 0 = none; I = inconstant; - = not available.

ing blood-pressure determinations at each clinic visit during a twenty-minute rest period, placebo treatment and, in addition, the method of having the blood pressure taken at home by an adequately instructed person or by the patient himself. In most cases, home observations were made both before and after operation. Postoperative observations were made almost continuously in some cases over a three- to five-year period. All blood-pressure readings, unless otherwise indicated, were made with the patient seated, the arm resting on a table.

Further standard methods of study included intravenous pyelography, sedative tests, pressor tests (breath-holding¹³ and ice water¹⁴), electrocardiograms, seven-foot roentgenograms, observations of the ocular fundi, postural tests^{9, 15} and renal-function tests (nonprotein nitrogen, phenol-sulfonephthalein and dilution-concentration). Most of these tests were repeated postoperatively, usually once a year.

DETAILS OF CASES STUDIED

Fourteen cases were studied before and after sympathectomy. In Table I are listed the preoperative and some of the postoperative findings in each case. In Case 14, death occurred a few days after operation. Cases 1, 5 and 6 were not studied preoperatively by the home method but have been evaluated by the usual clinical methods and in addition twenty-minute rest periods. This table also shows that observations were detailed and were made over a long period. The patients represent all stages of hypertension, including 2 cases with papilledema. The heart was either normal in size or only slightly enlarged. The electrocardiograms varied from normal to the usual signs of left-ventricular strain. The patients in Cases 10 and 11 had attacks of angina pectoris on exertion; those in Cases 1, 7, 11 and 12 had cerebral hemorrhages during the preoperative period. The patient in Case 6 was the only one with renal failure. All the patients were under the age of fifty years at the time of operation.

NUMBER AND TYPES OF OPERATIONS EMPLOYED

In Tables 2 and 4, it is seen that sympathectomy was performed in every degree of extensiveness. At the outset of the study, bilateral, two-stage supradiaphragmatic splanchnicectomy with resections of the tenth, eleventh and twelfth dorsal sympathetic ganglions was performed in 10 cases. In Case 4, an interval of four months with home and clinic study elapsed between the first and second stages, permitting evaluation of the unilateral operation. In 6 of these 10 cases, after adequate evaluation of the initial bilateral operation, further sympathectomy was done: a two-stage bi-

lateral infradiaphragmatic resection of the first, second and third lumbar ganglions. In Case 7, this was followed by three more operations, in which the stellate ganglion and the dorsal ganglions through the eighth were removed on the right side, and the lower inferior cervical and first, second, sixth, seventh, eighth and ninth dorsal ganglions on the left side. This represented an almost total sympathectomy. In Case 10, a left supradiaphragmatic splanchnicectomy and a right dorsolumbar transdiaphragmatic splanchnicectomy were done. The latter consisted of the removal of the ninth, tenth, eleventh and twelfth dorsal ganglions, the first lumbar ganglion and the splanchnic nerves.¹¹ Finally, in Cases 12 and 13, a bilateral dorsolumbar transdiaphragmatic resection was done, an interval of seven weeks of home and clinic study elapsing between the two stages in Case 12. We are greatly indebted to Dr. Reginald H. Smithwick for the performance of all the operations.

RESULTS OF SYMPATHECTOMY

Blood-Pressure Levels

The chart (Fig. 1) of a successful case (Case 11) will first be discussed, and the details of our preoperative and postoperative methods and findings will be explained. This forty-four-year-old woman was first studied in our clinic from December, 1937, to April, 1938. At each clinic visit, she was seated in a quiet room, and blood-pressure readings were taken by one of us at the start of and during a twenty-minute rest period. Between readings, the patient was left alone. During these four months of study, the blood pressure varied markedly, but it can be seen that it averaged 240/124 (240 systolic, 124 diastolic). During the next two-and-a-half-month period of study, the twenty-minute rest periods were continued, placebo treatment was given, and the home blood-pressure method was started. A friend of the patient was taught to take her blood pressure and did so at morning and night. At each sitting, three or four readings were taken during a five-to-ten-minute period. During this time, the clinic readings, indicated by the vertical heavy columns, averaged 224/124; the home readings, shown by the continuous wavy lines, averaged 200/114. During this period, the patient had a mild cerebral hemorrhage with hemiplegia.

The first set of operations was a two-stage bilateral supradiaphragmatic splanchnicectomy consisting of resection of the greater splanchnic nerves and the tenth, eleventh and twelfth dorsal sympathetic ganglions. The patient was followed postoperatively for three months, during which the average clinic readings were 214/124 and the average home readings 184/114. It is clear that

the operations had little effect on the level of the blood pressure. The patient was then subjected to a two-stage bilateral lumbar sympathectomy in which the first and second lumbar ganglions were removed. Following this step, there was a dramatic drop in all readings, so that the average clinic readings became 156/100 and the average home readings 124/80. This change has persisted

blood pressure was only slightly lower than before operation, running in the clinic at an average of 216/108 and at home at an average of 194/104. After a left dorsolumbar sympathectomy was done, a striking drop occurred; the average clinic levels became 140/84 and the average home levels 110/70. These levels have persisted up to the time of writing, a period of three and a quarter years

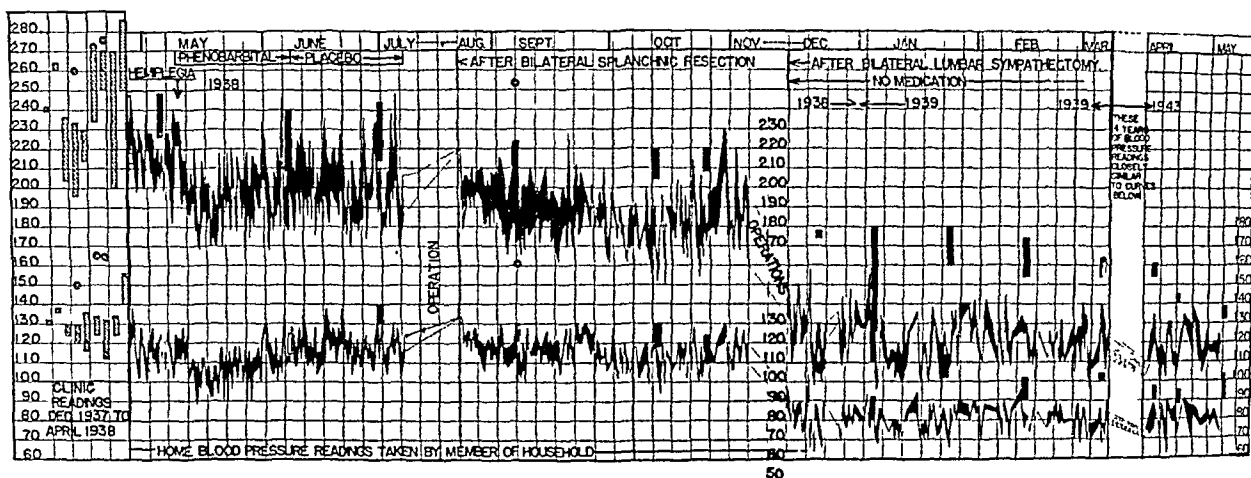


FIGURE 1. Case 11.

This chart shows five and a half years of preoperative and postoperative blood-pressure observations. The jagged continuous lines represent the home levels of blood pressure. The vertical columns, hatched or solid, indicate the clinic blood-pressure readings over a twenty-minute rest period. The end of the chart shows the last two months of 1943. The period between 1939 and 1943 is omitted for the sake of space, but the levels were unchanged.

to the present time. The end of the chart shows the readings during the last two months (April and May, 1943). The areas between 1939 and 1943, not charted, show exactly the same levels. The patient has continued taking her home readings, and has estimated that about eleven thousand readings have been made in the past five years; we have taken about one hundred and fifty clinic readings since the operation. This patient, unable to work more than four months a year prior to operation, is now working full time at the Boston Navy Yard.

Figure 2 presents the record of Case 12. The average levels of blood pressure rather than all the readings available have been plotted. The patient was a forty-eight-year-old woman who, prior to the beginning of this study, had a cerebral hemorrhage with good recovery. During one year of observation in the clinic with twenty-minute rest periods, the average blood-pressure levels were 220/120. Then, home readings taken by the patient were instituted, and over a four-month period the clinic levels averaged 250/120 and the home readings averaged 220/114. A right dorsolumbar sympathectomy was done and resulted in a pneumothorax. The patient convalesced for seven weeks. During this period, the

after the last operation. The patient now performs all the duties of an active housewife.

Figures 1 and 2 indicate how most of the patients were studied so far as the levels of blood pressure are concerned. Table 2 lists the results in the remaining cases, using the average levels or trends of blood pressure. This table indicates that, in the majority of the cases observed, the results were unsatisfactory. It also shows the different types of operations done in each case. The numbers to the left of each blood-pressure reading indicate the length of observation in weeks, months or years that the average reading covers, and applies to both the clinic and the home readings during this period. Thus, in Case 3, the blood pressures taken for seven weeks in the clinic with twenty-minute rest periods averaged 230/146; for the next six weeks, the average readings in the clinic were 228/138 and the average home readings 222/136. After completion of the two-stage splanchnicectomy, the patient was followed for seven months up to his death, and during this period the clinic blood pressures averaged 236/144 and the home readings about the same, 226/136. It is clear, therefore, that this patient was not benefited by the operation so far as the blood-pressure levels are concerned, and

his death seven months after the operation indicates that the sympathectomy did not have any discernible effect on the progress of the disease. This case was one of Group 4 (Keith-Wagener¹⁰)

The patient had a pneumothorax and so was allowed home for four months before the other side was done. It is seen that the unilateral operation had little or no effect on the blood-pressure levels,

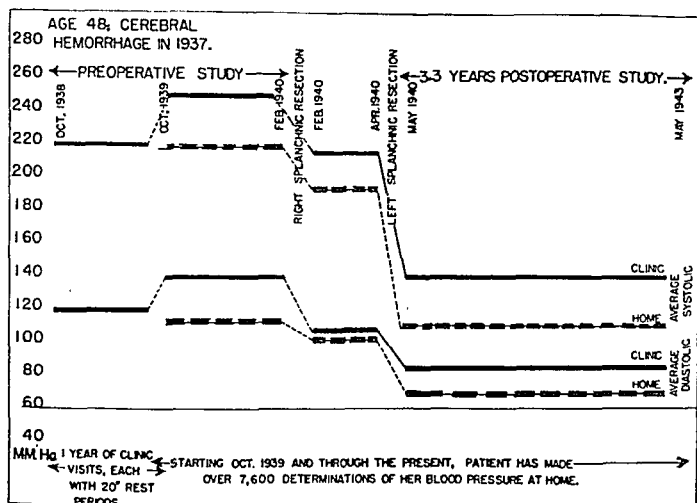


FIGURE 2. Case 12.

This chart shows the preoperative and postoperative average levels of blood pressure. The clinic levels are indicated by the solid black lines, and the home levels by the broken black lines. A period of seven weeks at home elapsed between the first and second stages of operation. The operation performed was the transdiaphragmatic dorsolumbar sympathectomy (Smithwick type).

hypertension with papilledema; headaches were improved after operation.

Efficacy of Type of Operation

Supradiaphragmatic splanchnicectomy. Of the 10 cases in which bilateral supradiaphragmatic splanchnicectomy was done as a first attempt to lower the blood pressure (Cases 1, 2, 3, 4, 5, 6, 7, 8, 9 and 11), only 1 case (Case 8) showed a significant drop in the clinic blood-pressure readings. We have arbitrarily chosen a minimum drop of 30 mm. systolic and 14 mm. diastolic as minimum evidence of any effect of the operation on the levels of blood pressure in the clinic or home. Turning to the home levels of blood pressure in these 10 cases, it is noted that Cases 4, 7, 8 and 9 showed significant drops in blood pressure. However, in only 1 case (Case 9) did the average blood-pressure level drop to normal. Case 4 in Table 2 is worth noting with reference to the findings after only one side of the splanchnicectomy was done.

but that when the left side was operated on, there was a definite drop in the home levels, persisting for the next five years. If these cases are analyzed to compare the relation of effect of operation to grade of hypertension, it is found (Table 3) that the only case with a significant effect in the clinic level of blood pressure was of Grade 2. By the home method, 3 additional cases were found to have a drop, and these were Grade 2 or 3. It is unfortunate that in 2 of the 3 cases of Grade 4, there was no opportunity to have home observations made. In Case 5, which is labeled in Table 3 as having a questionable result, there was a brief period of home readings a year after operation. The home readings in this case were much lower than the clinic readings. As evidence of possible effect of operation, this case showed a marked postoperative change in the electrocardiogram: a deeply inverted T wave in Lead 1 gradually changed to an erect T wave, depressed ST in-

tervals in Leads 1 and 2 became normal, and an inverted T wave in Lead 4 became erect.

Supradiaphragmatic splanchnicectomy followed by lumbar sympathectomy. Table 2 indicates that of the 10 cases first subjected to splanchnicectomy,

and 8). Of these 6 cases, only 1 (Case 11) had a drop in clinic level and a drop to a normal level by the home observations, lasting four and a half years to the present. Case 8 continued to maintain the improvement in clinic readings produced



FIGURE 3. Case 5.

Three sets of electrocardiograms, taken in June, 1937, in March, 1938, and in May, 1943, respectively. During this period, although the T waves in Lead 1 became normal, there was no improvement in the blood-pressure levels obtained at the clinic.

6 (Cases 1, 4, 6, 7, 8 and 11) later underwent more extensive sympathectomy. In these cases, the further operations were two-stage bilateral infradiaphragmatic lumbar resections in which the first and second and occasionally the third lumbar ganglions and the sympathetic trunks were removed. These lumbar operations were performed at intervals varying from four weeks to one and a half years after the original splanchnicectomies. They were done because of failure of the original operations (Cases 1, 6, 7 and 11) and to observe whether more extensive removal of the sympathetic system would be more effective (Cases 4

by splanchnicectomy, and also showed a further drop in the home readings after the lumbar operations. On the whole, therefore, the addition of the lumbar operations in these 6 cases produced a beneficial effect in 2 cases (Grade 2 and 3). Table 3 shows that of the 4 unbenefited cases, 2 were Grade 4 and 2 were Grade 3.

Total sympathectomy. Total sympathectomy was carried out in only 1 case (Case 7). This patient was subjected first to supradiaphragmatic splanchnicectomy, then to resection of the lumbar ganglions, and then to three more stages in which the stellate ganglions down through the eighth

TABLE 2. Average Preoperative and Postoperative Blood Pressure Levels

CASE No	PREOPERATIVE READINGS				POSTOPERATIVE READINGS						REMARKS	
	BEFORE HOME STUDY		AFTER HOME STUDY		AFTER SYMPLECTIC OPERATION		AFTER DORSOLUMBAR OPERATION					
	period	mm /Hg	period	mm /Hg	Unilateral period	Bilateral mm /Hg	Unilateral period	Bilateral mm /Hg	Unilateral period	Bilateral mm /Hg		
1	3 wk	210 110	-	-	-	1½ yr	230 120	-	1 yr	200 120	Death from cerebral hemorrhage	
2	1 yr	246 122	-	-	-	4 yr	222 124 206 112	-	-	-	Death from acute pulmonary edema and coronary occlusion	
3	7 wk	230 146	6 wk	228 138 222 136	-	7 mo	236 144 226 136	-	-	-	Death from cerebral hemorrhage	
4	-	-	3 mo	230 134 190 114	4 mo	230 138 170 130	8 mo	196 142 150 110	-	4½ yr	220 130 150 110	
5	6 mo	234 132	-	-	-	5¼ yr	230 130 184 106	-	-	-		
6	2 mo	190 120	-	-	-	2 mo	170 120	-	7 mo	200 140		
7	1 yr	224 146	4 wk	220 144 210 134	-	4 wk	192 134 180 120	-	1 mo	206 144 194 132	4½ yr after total sympathectomy clinic, 114 home 176 114	
8	-	-	6 wk	196 136 196 136	-	2 mo	150 114 150 116	-	4½ yr	142 106 130 100		
9	3 mo	194 114	7 mo	200 112 164 88	-	4½ yr	178 108 126 76	-	-	-		
10	-	-	3 mo	220 126 204 112	-	-	-	-	4½ yr	158 100 124 80		
11	4 mo	240 124	3 mo	224 124 200 114	-	3 mo	214 124 184 114	-	4½ yr	156 100 124 80		
12	1 yr	220 120	4 mo	250 140 220 114	-	-	-	7 wk	216 108 194 104	3½ yr	140 84 110 70	
13	-	-	7 mo	206 136 184 110	-	-	-	-	1½ yr	136 94 108 64		

In each column of blood pressure readings the upper set is the clinic reading and the lower set the home reading.

dorsal ganglion on the right and the inferior cervical and first, second, sixth, seventh, eighth and ninth dorsal ganglions on the left were removed — an almost total sympathectomy. A small area of sweating over the left anterior chest confirms the

readings, the full drop did not appear until three weeks after hospital discharge. The delay in drop seemed related to pain about the operative scars. In the unsuccessful cases, followed up to five years, there has been no evidence of any tendency toward

TABLE 3. Results of Different Operations Compared with the Severity of the Hypertension (Keith-Wagener¹⁶).

TYPE OF OPERATION	EFFECT ON BLOOD PRESSURE	SEVERITY OF HYPERTENSION					
		GRADE 1	GRADE 2	GRADE 3	GRADE 4		
Supradiaphragmatic splanchnicectomy and dorsal ganglionectomy	Clinic		0 + 0	0 0 0 0	0 0 0		
	Home		10 + +	0 + + 0	- 0 -		
	Case No.		5 8 9	2 4 7 11	1 3 6		
Above with lumbar ganglionectomy	Clinic		+	0 0 +	0 0		
	Home		++	+ + +	- -		
	Case No.		8	4 7 11	1 6		
Transdiaphragmatic lumbodorsal splanchnicectomy (Smithwick)	Clinic		+	+ +			
	Home		+	+ +			
	Case No.		13	10 12			

persistence of the third, fourth and fifth dorsal ganglions. Table 2 shows that for the past four and a half years since completion of this extensive denervation, the blood pressure has been somewhat lower, both in the clinic and the home, but nowhere near normal. Further details of this unusual case will be published elsewhere.

Transdiaphragmatic lumbodorsal splanchnicectomy. This was done in Cases 10, 12 and 13 by the

lowering or elevation of the blood pressure. In the successful cases followed postoperatively as long as four and three quarter years, there has been no tendency of the blood pressure to rise in either home or clinic readings.

The correlation of postoperative effect with preoperative sedative test with Sodium Amytal has not been good. The patient in Case 7, on whom the total sympathectomy was performed, had a

TABLE 4. Effect of the Different Types of Sympathectomy on the Clinic and Home Levels of Blood Pressure.

TYPE OF OPERATION	NO. OF CASES	NO. OF CASES WITHOUT ANY EFFECT	NO. OF CASES WITH GOOD EFFECT ON CLINIC LEVELS	NO. OF CASES WITH GOOD EFFECT ON HOME LEVELS	NO. OF CASES WITH NORMAL HOME LEVELS
Supradiaphragmatic splanchnicectomy	10	6	1	4	1
Above operation followed by infradiaphragmatic lumbar operation	6	4	1	2	1
Total sympathectomy	1	0	1	1	0
Transdiaphragmatic lumbodorsal splanchnicectomy and so forth	3	0	3	3	3
Total end results			5	9	5

Smithwick method. Case 10 had a left supra-diaphragmatic splanchnicectomy and a right trans-diaphragmatic operation. The patients have been followed postoperatively from one and a half to four and a half years. All had a marked drop in clinic levels close to normal, and a complete drop to normal in their home readings taken daily up to the present. Two of these cases were Group 3 and one was Group 2.

Additional Points Regarding Blood-Pressure Levels

In all cases in which a marked drop in blood pressure occurred, the fall in the clinic readings appeared immediately after operation. This rapid drop also occurred in the home readings in all cases but 1 (Case 9). In this patient, although there was some drop at the outset in the home

sedative drop in blood pressure to 96/66, but had little postoperative drop.

We should like to emphasize the constant instability of the preoperative and postoperative blood pressure levels in our cases. Although the figures in Table 2 report the averages of thousands of home readings and hundreds of clinic readings, such average figures merely represent trends. The actual facts are illustrated in Figure 1. In this case, although the average clinic readings after operation are 156/100, in reality they varied from 180/112 to 128/80 and the home readings, which averaged 124/80, varied from 140/94 to 92/58. Similar fluctuation at higher levels is evident preoperatively in this chart. There were, therefore, swings in blood pressure postoperatively amounting to as much as 88 systolic and 54 diastolic. The lower

levels usually occurred after sitting and resting a few minutes or were found oftener in the morning. If our cases were reported on the basis of readings after resting only, it is evident that the selected level would be much lower. The higher clinic and home levels were usually related to environmental or emotional stimuli. Finally, in only 1 patient (Case 12) was the blood pressure often normal as soon as she entered the clinic and sat down. Even in this case, elevated readings were frequent when she first sat down, and dropping to or near normal after twenty minutes of rest.

Postoperative Complications

Pneumothorax due to inadvertent nicking of the pleura occurred in 3 cases, but had only a brief effect on complete rapid recovery from the operation. In Case 14, death resulted three days after the first stage of a supradiaphragmatic splanchnicectomy from an overwhelming streptococcal infection of the mediastinum. In Case 10, unusual spells, apparently unrelated to the operation, developed eight months after operation. These episodes consisted of generalized shaking either when the patient was asleep or, less often, awake, with twitching of the face and inability to talk. The diagnosis has been the subject of debate by several neurologists; hysteria and diencephalic epilepsy have been considered. Electroencephalograms were within normal range, and spells did not respond to Dilantin Sodium or to phenobarbital. The fact that they developed eight months after operation and that the blood pressure was lowered makes it unlikely that they were related. Reactions of this nature have not been reported in papers on sympathectomy. Sterility in men due to inability to empty the seminal vesicles may occur when the lumbar ganglions are removed. Our own data on this point are inadequate.

Postural Changes in Blood Pressure and Pulse

As noted by Roth¹² and Allen and Adson,⁹ extensive denervation is associated with a marked drop in blood pressure and with tachycardia when the patient stands. This occurred in marked degree in Cases 11, 12 and 13, and in a mild degree in Cases 7, 8 and 10. In Case 7, however, a moderate postural effect on blood pressure was unassociated with any pulse rise; in fact, the pulse remained around 50. In all cases, the postural effect wore off in two or three months. It is of significance, however, that in patients whose home readings while seated at times have been as low as 76 systolic, there has been no tachycardia or faintness even four years after operation.

Changes in Heart Size and in Electrocardiograms

Table 1 shows that in only 4 of the 13 cases (Cases 5, 6, 11 and 12) was there any cardiac en-

largement before operation, and this was of only slight degree. In Case 6, death from renal failure occurred. The remaining 3 patients are still living. In Case 5, the enlargement has remained unchanged over the five and a quarter years of postoperative observation. During this period, the electrocardiogram has become normal. In Cases 11 and 12, which originally showed slight enlargement, the heart has returned to normal size. Even in some of the cases showing normal heart size before operation, serial x-ray films have revealed postoperatively a definite decrease in size. There have been no cases with increase in heart size postoperatively.

Table 1 also shows which cases had preoperative and postoperative electrocardiographic abnormalities. In Cases 5 and 10 the T waves in Lead 1, inverted before operation, postoperatively became erect (Fig. 1). In Case 5, this was unassociated with any evidence of improvement of blood-pressure level in the clinic. In this case, home readings were available over only a brief period postoperatively; they were moderately lower than the clinic readings. In Case 12, the T waves in Lead 1, inverted to a depth of 7 mm. preoperatively, showed after operation inversion to a depth of 2 mm.; in Lead 2, the T waves, previously inverted, became erect. In both Cases 10 and 12, the changes were also associated with the development of deep Q waves in Lead 3. Case 10 had angina pectoris preoperatively on exertion; it has not recurred in the four and three-quarter years since operation. The ST intervals were depressed preoperatively in Leads 1 and 2 in Cases 5, 10 and 12, becoming normal after operation. In Cases 10 and 12, the clinical result was excellent. Left-axis deviation did not change more than slightly following operation, but any expected decrease was probably prevented by a gain in weight of twenty to thirty pounds in these two cases.

Changes in Eyegrounds

In 2 cases (Cases 1 and 3), there was edema of the optic disks. In Case 1, the edema disappeared postoperatively and did not recur in the two and a half years that elapsed before the patient's death. In Case 3, death occurred seven months after operation; unfortunately, the postoperative records of the fundi were lost. In the other cases, no definite change in any direction was noted after operation. The ophthalmologist was occasionally of the opinion that the vessels seemed wider after operation (Case 13). Arteriovenous nicking and changes in caliber have not improved. No evidence of progress is present in the patients who are still alive.

Changes in Renal Function and Albuminuria

The renal function was normal in all cases except 1 (Case 6). The latter showed preoperatively an elevated nonprotein nitrogen, with a fixed specific gravity of the urine and constant albuminuria. Of the 4 patients with constant albuminuria preoperatively (Cases 1, 3, 6 and 8), 2 (Cases 1 and 3) died of cerebral hemorrhage, 1 (Case 6) died of renal failure, and 1 (Case 8) is still living. The last patient has had a good operative result. Of 3 patients with inconstant albuminuria, all are living, and only 1 has had a strikingly successful result.

Intravenous pyelograms were normal in all but 2 cases (Cases 8 and 11). In Case 8, there was a history of pyelitis of pregnancy in 1929, with a kink of the right ureter straightened by operation. A pyelogram taken before the sympathectomies showed some blunting of the calyces and slight enlargement of the pelvis of the right kidney. In Case 11, pyelograms and flat plates revealed a small right kidney with only slight function. It is striking that in both these cases with abnormal pyelograms, sympathectomy produced excellent results lasting up to the present. In Case 11, two years after sympathectomy, the right kidney was removed because of pain; it was found to be hypoplastic and atrophic, with chronic pyelitis. The blood pressure, normal before nephrectomy, remained unchanged after nephrectomy.

In general, no improvement was noted in the concentrating ability of our cases.

Symptoms before and after Operation

Table 1 indicates apparent symptomatic improvement in many cases. The chief symptom relieved was headache. This occurred even when there was no apparent improvement in blood pressure. Only 1 case (Case 7) was free of symptoms before and after operation. In 1 case (Case 2), symptoms were more marked after operation. The patients in Cases 8, 11, 12 and 13, almost wholly incapacitated before operation, have returned to full activity since operation. The other cases did not show any striking improvement in capacity for work.

Pressor Tests before and after Operation

We have carried out many pressor tests, using the breath-holding and ice-water methods. They have not been of any aid preoperatively and have added little to our findings postoperatively. Whether or not the operation is successful, the pressor test may show no change in range—the range meanin^g the amount of rise in blood pressure produced by the test. Some successful cases,

however, may have a postoperative decrease in range. The top level to which the blood pressure rises after the pressor tests is called the ceiling; this is lower in benefited cases, but the success of operation is easily seen in the top clinic readings themselves. On the other hand, the pressor-test ceiling after the operation and occasionally preoperatively may be much less than the actual height at which the blood pressure is frequently found in the clinic without pressor-test stimulation. Case 12 is an example. Although this patient has become a so-called "hyporeactor" to the tests,—that is, a normal range,—the readings in the clinic varied markedly: at one visit she might have a top blood pressure of 196/104 and at another visit a top reading of 130/80. These top readings in the clinic were much higher than the ceilings obtained by the pressor tests. It is clear, therefore, that the pressor tests do not indicate the degree to which the blood pressure in some of these patients fluctuates. In other words, the range of blood pressure after pressor stimuli of breath-holding or cold is much less in such cases than the range produced by environmental stimuli

COMMENT

Regardless of how skeptically and critically we have viewed less well-controlled studies of sympathectomy, our own data, viewed just as critically, have convinced us that no medical therapy has ever equaled the results obtained in 5 of our 13 cases. Certainly, the blood pressure can be lowered to a marked degree by potassium thiocyanate in large, somewhat toxic doses, and kept down for prolonged periods, but constant attention must be given to such patients, and their activity becomes greatly depressed by the marked effects of the drug.^{17, 18} A patient can be ordered to bed and given large doses of sedatives with a similarly good effect on the blood pressure. It is clearly recognized that but little has been accomplished in the medical treatment of this disease. No one can point to a single well-controlled case in which medical treatment has brought the size of the heart, the electrocardiogram and the blood pressure back to normal. In our experience, sympathectomy has accomplished this in some cases with persistence of success for five years to the time of writing.

The optimism and enthusiasm rising out of our findings have been tempered by some provoking facts and queries. First, the operation, no matter how extensive, has not, even in our most successful case (Case 12), abolished rises in blood pressure produced by excitement. Almost one hundred thousand home readings of the blood pressure show rises associated with arguments, great

physical or emotional strain, markedly cold rooms and so forth. The average home existence of these patients does not often produce such rises, and the blood pressure may be as low as 80/64. In the clinic, the initial readings taken immediately after the patient enters the examining room are oftenest in the abnormal levels, even if on resting they drop to or close to normal. These marked variations of blood pressure indicate that large underventilated areas are left and that the hypertensive tendency still exists. The fluctuations in blood pressure in these patients resemble those seen in many young, early hypertensive patients who used to be dismissed with the diagnosis of emotional hypertension.

The promising picture presented in this paper must be viewed in the light of this question: Does the operation increase the life expectancy in the successful case? Our own data do not, of course, contribute an answer. Other reports are strikingly conflicting. Woods and Peet,¹⁹ on the one hand, state that splanchnicectomy does increase life expectancy, and Flaxman²⁰ on the other, after comparing Woods and Peet's results with medically treated cases, concludes that there is little difference in mortality between the two groups. Even if the latter theory proves to be correct, results like those in Cases 10, 11, 12 and 13 justify the operation merely on the ground that it makes possible for the patient such long periods of normal activity and well-being.

We must also take cognizance of the argument raised by Volini and Flaxman²¹; namely, that hypertensive patients often have a drop in blood pressure after any major operation. This is reasonable if one remembers that great inactivity and some asthenia after major operations do cause a lowering of the blood pressure. The present study, however, clearly indicates that this is not the reason for the drop in blood pressure in our cases. First, the drops in blood pressure were not transitory, but have persisted up to five years. Secondly, in Cases 4, 11 and 12, intervals of months elapsed between stages, and the precipitous drop in blood pressure did not occur after the first stages while the patients were up and about convalescing. Finally, there is evidence that extensive sympathectomy carried out in patients with normal blood pressure has practically no effect on the readings, even in the upright position.¹⁶ In this sense, the effect of sympathectomy on the blood pressure of essential arterial hypertension is a specific one and not comparable to the effect of transitory asthenia and inactivity following operations in general.

Another disturbing fact is that 5 of our 13 cases failed to respond successfully. Since our patients were operated on by a surgeon highly skillful in

sympathetic-nerve surgery, we are certain that the amount of sympathetic resection planned preoperatively was carried out. This leaves, therefore, two explanations of failure: first, the cases with extremely severe forms of the disease did not respond, or secondly, the operation was not sufficiently extensive. Certainly, the newer operation — transdiaphragmatic splanchnicectomy — has had a more constant degree of success. On the other hand, the slight response to an almost total sympathectomy in a Grade 3 hypertensive patient indicates that there are other as yet undiscovered reasons for failure.

So far as the failures reported in the literature are concerned, our studies indicate an additional important reason for some of the apparently poor results. We believe that, as in Cases 4, 7, 8 and 9, some of the cases reported in the literature have had a much better result than the clinic readings of the blood pressure indicate. We feel certain that, as in our own cases just cited, there are many cases in which the home blood-pressure readings have been lowered greatly since operation, although the clinic readings have been lowered little or not at all. This is a probable explanation for the change of the electrocardiogram to normal in Case 5. It seems also a likely explanation for the report of Bordley et al.²² that in one of their cases there was a decrease in the size of the heart, the electrocardiogram lost its left-axis deviation for two years, and there was no improvement of the blood pressure after operation. It may also explain why many cases have improved symptomatically without any apparent change in blood pressure.

Several more questions will inevitably be raised. First, what is the value of the home blood-pressure method? As stated in previous papers, we believe that it is invaluable for the true interpretation of any therapy in hypertension. In no cases have we seen any psychic harm from the use of the method. A second question that may be raised is, If the patients who have normal blood-pressure readings at home also have rises on excitement, what do the normal home readings really represent? We think that the home readings represent the usual level of blood pressure during the patient's normal life at home. Otherwise, we should have found hundreds of high home readings among the thousands taken in a given case if the levels were raised by merely slight happenings at home. The clinic or office high readings, therefore, represent the excitement associated with a visit to the doctor. It is provocative to note and emphasize that this excitement may produce after operation a rise in blood pressure much greater than that produced by the pressor tests.

The question of the effectiveness of surgery in relieving symptoms must be considered separately, since so much of the subjective factor enters into the picture. The evaluation of symptom relief is most difficult. We² have already shown that any strong form of suggestion treatment is markedly effective in relieving symptoms. This should be kept in mind in cases where relief of symptoms has occurred in the absence of any demonstrable effect on the levels of blood pressure. We disagree strongly with the statement that the operation is justified merely for the relief of distressing symptoms, even if the good results last only several months, and that the criteria for operation are incapacitating symptoms.

We now believe that the criteria for operation are severe or progressive disease in which there is no renal or cardiac failure, and the development of any of the following: cardiac enlargement, electrocardiographic evidence of left-ventricular strain, inconstant or constant albuminuria and marked changes in the ocular fundi. The age factor is a matter not yet settled; it seems to us that as time goes on, one must seriously consider those people over fifty-five years of age who now receive no attention. Chronic unilateral renal disease is not a contraindication (Cases 8 and 11). Time may prove the same to be true for bilateral renal disease.

Three final points are as follows. The preoperative and postoperative evaluation of such cases should be the primary concern of the internist. The decision to operate should rest on the opinions of the internist and surgeon and the patient as well. In suggesting surgery to such patients, the experimental nature and uncertainty of success should be made clear. Finally, the operation should be performed only by surgeons who are properly trained in this field.

SUMMARY AND CONCLUSIONS

There have been presented a small series of patients with essential hypertension who have undergone a variety of sympathetic denervations and who have had the advantage of unusually detailed controlled study. This type of controlled study with sympathectomy has not been secured or reported before. The controls consisted of special clinic study of the blood pressure, together with home blood-pressure determinations by the patients themselves.

The data so gathered lead inevitably to the conclusion that sympathectomy, regardless of its rationale, is the first therapy of essential hypertension that has been shown to produce in some cases a marked, prolonged, nontoxic lowering of the blood pressure. With this improvement in blood pres-

sure, the heart may gradually decrease in size, the electrocardiogram return to normal, the symptoms disappear, and the incapacity be replaced by completely normal activity lasting at least as long as five years. Angina pectoris may disappear. Successful sympathectomy did not result in constantly normal blood-pressure levels in any case.

Our study does not completely clarify the reasons for failure but does offer some explanations. First, regardless of the extent of sympathectomy, Grade 4 patients did not respond. Secondly, success in general was more constant in those patients subjected to extensive denervation. The transdiaphragmatic type of splanchnicectomy with dorsolumbar ganglionectomy was the most effective type of operation. Finally, some failures are only apparently so when judged by the standard clinic readings of the blood pressure, whereas the home blood-pressure method reveals real improvement.

Therapy by sympathectomy should be considered in patients with essential hypertension in whom progressive elevation of the blood pressure is found after long and careful study or in whom any evidence of beginning vascular damage is demonstrated. Proper control figures of blood pressure levels and variations should be secured, preferably in the ambulatory state. Brief periods of preoperative hospitalization do not afford proper data with which to compare postoperative results, no matter how many intricate or detailed studies are carried out during such periods. In a disease that has usually existed for some years, there is only rarely an excuse for brief preoperative studies or emergency decisions. Such studies and decisions are the primary concern of the internist.

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SOCIOECONOMIC ASPECTS OF DISEASE*

A Community Study of Pulmonary Tuberculosis in Selectees

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ALTHOUGH it has long been recognized that the incidence of pulmonary tuberculosis is especially high in crowded slums, and that certain races apparently have greater susceptibility than others to this disease, the exact effect of these factors has never been properly weighed and differentiated. As our examination of selectees before induction into the armed forces includes routine chest roentgenograms, an unparalleled opportunity has been offered for studying the incidence of pulmonary tuberculosis in men of military age coming from communities of different types. The purpose of this study is to correlate the prevalence of pulmonary tuberculosis in selectees with the factors of the socioeconomic level, population density, nationality and industries of the communities from which they came.

One of the best determinations of the relation of tuberculosis to economic level was that of the National Health Survey,¹ which showed that the rate of disability from tuberculosis is nine times as high for those on welfare as that for persons in the upper income group of \$3000 per year and over, and almost four times as high for those with annual incomes of less than \$1000 as for those with incomes of \$3000 and over. Hart and Wright² in their studies in England, in addition to pointing out the similarity between the curves of pulmonary tuberculosis and of real earnings, noted the effect of differences in average closeness of personal contact between the inhabitants in one county borough and those in another. Other studies of the relation of tuberculosis to popula-

tion density consist largely of the comparison of urban and rural rates. Parkhurst³ in 1933 found the total rural rate to be 15 per cent lower than the urban rate, and Sydenstricker⁴ during the period of 1900-1915 found the urban rate maintained at double the rural rate. Whitney⁵ reported that the death rate from tuberculosis is more than twice as high in laboring classes and factory and mill workers as in business and professional people and farmers. Dauer⁶ states that numerous reports have demonstrated that immigrants from certain countries to the United States have higher tuberculosis death rates than do the offspring of native-born parents. The Irish have had especially high rates, whereas the Italians, Russians and Jews have had relatively low rates.

No paper has appeared that differentiates the effects of low economic status and crowded housing. Although it is obvious that these two factors are often found together, their relation is not constant, and a differentiation of them is important in the establishment of mass preventive methods. In this paper an attempt will be made to differentiate the effect of population density and that of the socioeconomic level.

Although it has been stated that the high incidence of tuberculosis in the foreign born and their children and in certain races may have been influenced by their low economic status and the crowded housing of immigrant communities, it has not been shown that the latter are not the prime causative factors rather than racial susceptibility, to which the high incidence was attributed. Our consideration of the relation of economic status and population density to the prevalence of tuberculosis in certain nationalities is far from complete, but it does suggest a method for

*From Headquarters Boston Armed Forces Induction District. Presented at a meeting of the Massachusetts Trudeau Society, Boston, May 14, 1943.

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isolating the various factors contributory to the incidence of tuberculosis.

At this time it is possible to review the findings for almost the entire period of Induction Board examinations from December, 1940, until early in 1943. Of the selectees who received chest roentgenograms at the Boston Armed Forces Induction Station during this long period, 0.9 per cent were found to have pulmonary tuberculosis. Sixty-six per cent of these did not know that they had the disease. Of the cases that it has been possible to follow, 60 per cent have shown pulmonary tuberculosis in an active stage.

METHOD OF STUDY

Every selectee as a part of his examination has a routine chest photoroentgenogram at the Induction Station. Only the cases classified as pulmonary tuberculosis, reinfection type, are considered here. The diagnosis is made by an accredited radiologist on x-ray evidence, in most cases on the basis of four-by-five-inch stereoscopic photoroentgenograms, except occasionally when the radiologist desires single or stereoscopic fourteen-by-seventeen-inch films for verification. Rarely has this been found necessary, and then only in cases in which there were lesions of minimal extent of doubtful stability or in which measurement of the extent was necessary. Occasionally, the clinical history was inquired into, and this assisted in the diagnosis of doubtful cases. Before cases were classified as pulmonary tuberculosis, the films were reviewed by one of us (D. Z.). Tuberculosis suspects were not included as cases unless they were later proved to be tuberculous.

The men examined during most of the period were selectees between the ages of twenty-one and thirty-eight, some in the eighteen to twenty-one and thirty-eight to forty-five age groups were examined during part of the period. Because of its youth, the former age group is not presented as representative of the population in general, but it does form an excellent cross section of the male population of draft age without dependents, not engaged in essential industry, and not possessing obvious disqualifying defects evident on inspection by local-board examiners. Two groups not submitted as selectees and hence not included are those men who passed the physical examination for enlistment as volunteers in the armed forces and did not have tuberculosis, and those undergoing sanatorium treatment for tuberculosis, or, in rare cases, rejected by local boards because of proved tuberculosis. These two groups, one with, and the other without tuberculosis, tend to balance each other.

The source of the registrants was the eastern segment of Massachusetts at no point more distant than thirty miles from the coast line. The diversity of population represented was exceptional, ranging from high population densities, at their greatest in Boston proper and including four other cities of over 100,000 population and fourteen with more than 25,000, to such low densities as are represented in more than fifty towns and villages with a population of less than 2000. Industries of all types are found in the cities and large towns. Many semirural areas where the chief occupations are farming and fishing are represented. Many diversified nationalities are present, with the foreign population of Irish, Italian, Jewish and many mixed foreign groups concentrated especially in the urban areas, and with other communities still of almost purely English stock, now in the sixth and seventh generations in this country.

A social study was made of the area with the use of such available statistics as Lambie's *Experiments in Methods of Municipal Analysis*⁷ and *Social Statistics*⁸ of the Boston Council of Social Agencies, which together give detailed information on population densities, tax rates, welfare rates, industries, wages and a variety of other factors influencing the economy of the area. Surveys of the communities made by interrogation of many persons from each of them gave an evaluation of the utilization by the subject of the social and economic assets of his community and a subjective evaluation of the statistical data on the community. From these data a classification of each community was made covering the following factors: socioeconomic level (desirability), density of population per square mile, dominant nationality, and dominant occupations and industries.

The principle of our assessment of socioeconomic level of the community was based on Lynd's *Middletown*,⁹ wherein the social structure of an American community is intensively studied. The following factors were evaluated to obtain an index of socioeconomic level: medical care, educational facilities, density of housing, social class, recreational facilities, public works and welfare. These were chosen because, except for welfare, they represent those factors in a community that either influence or characterize its socioeconomic level. Welfare was used because it was the most objective figure available of economic level. This method of measuring community socioeconomic levels is considered superior to others because it is more universally applicable, is obtainable by a comparatively easy survey, and should be more consistently correct than an evaluation of any single factor such as basic wage, a figure that is

both difficult to obtain in certain areas and invalid at this time because of such special circumstances as high wartime wages.

The local board was used throughout as the community unit, and it fortunately is a satisfactory one, being comparable to a city ward, a large town or several adjacent small towns.

All communities were rated according to the above socioeconomic factors and placed in one of six groupings according to their socioeconomic level, ranging from A, the finest communities, to F, the slum areas. The tuberculosis rate on examination was found for each community and the total rate for the group was calculated.

In the separate consideration of correlation of tuberculosis with community welfare rates, the rates of 1936 to 1939 were used because they were considered more representative than any rates of today would be. All the communities were divided into four groups according to the welfare rates given by Lambie; namely, less than twenty, twenty to twenty-nine, thirty to thirty-nine and forty dollars or more per capita. Tuberculosis rates in these groups were calculated and compared.

Population density based on the number of inhabitants per square mile was found for each community sending selectees to this station. Communities were placed in seven groups according to population density, ranging from less than 500 to over 20,000 per square mile. In this way a complete study was made possible of the relation of tuberculosis incidence to population density. As the desirability rating previously described for every community was known, it was possible by considering the rating of any one density group to see what extent desirability influenced tuberculosis incidence in different population densities.

Because of the mixed nationalities that made up most of the communities, it was possible to consider only a small part of them in comparing various nationalities; hence, only those communities with a dominant nationality were grouped by nationality. The tuberculosis incidences in selectees from these groups were compared. Here the factors of the socioeconomic level and population density can be evaluated to see whether or not they explain the difference in incidence found.

A like consideration was made of those communities with a dominant industry, in an effort to show to what extent socioeconomic factors are related to the differences in the incidences of tuberculosis found in different industries.

All the communities studied were ranked according to their tuberculosis incidence. Seventeen communities were found to have especially high and seventeen especially low rates for tuberculosis. The characteristics of the seventeen com-

munities with the highest rates were compared with those of the seventeen with the lowest rates.

RESULTS

Tuberculosis Rate and Community Desirability

The correlation of tuberculosis incidence in selectees with the desirability rates of the communities from which they came is shown in Figure 1.

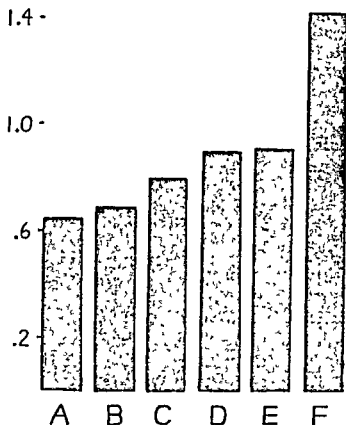


FIGURE 1. Incidence of Pulmonary Tuberculosis at Different Levels of Community Desirability, from A, the Best, to F, the Poorest.

Here the incidence of tuberculosis in selectees increased from 0.7 per cent in the best (A) communities to 1.4 per cent in the poorest (F). This doubling of the incidence of tuberculosis tends to confirm the findings of the National Health Survey¹ and the study of Hart and Wright² in England on the relation of tuberculosis to income. Their studies, however, were on an individual basis, correlating tuberculosis incidence with income, whereas this study rests on a community basis wherein a much poorer correlation would be expected.

To see if the same correlation was found with mortality as that with morbidity, the death rates for the years 1937-1941 for the same communities were compared. As good a correlation was shown as that for incidence, with the death rate ascending from 24 per 100,000 population in the most desirable (A) communities to 60 per 100,000 in the poorest (F).

The importance of this relation of pulmonary tuberculosis to socioeconomic level can in no way be minimized, especially in view of the fact that without doubt the public-health attack on tuberc-

culosis has not been neglected in those communities with the lowest socioeconomic level. For this reason it cannot be considered, as it might be in certain other diseases, simply as indicative of medical neglect, but must be associated more with low standards of living found in the undesirable areas. The fact that there was an incidence of pulmonary tuberculosis of 0.7 per cent in the finest communities is also notable, for such a

communities with populations less than 5000 per square mile, only five presented rates for pulmonary tuberculosis higher than the average. Communities of a great variety of types and qualities are represented among these forty-six communities, and the fact that only five had tuberculosis rates above the average indicates the extent to which low population density is associated with low tuberculosis incidence.

From population densities of 5000 per square mile up to those of over 20,000 per square mile, there was an ascending rate of pulmonary tuberculosis from 0.6 to 1.4 per cent. All but two of the fourteen communities with population density over 20,000 per square mile presented a tuberculosis rate above the average. This serves to illustrate what is considered to be the effect of crowded housing in a contagious disease such as tuberculosis, where close contact with active cases is conducive to its spread. These findings are in agreement with the work of Hart and Wright,² Parkhurst³ and Sydenstricker.⁴

A similar study of mortality made by comparing the tuberculosis death rates for five years in the various population densities yielded similar results. The death rates rose from 28 per 100,000 population in densities of under 2000 to 54 per 100,000 in those of over 20,000 per square mile.

It is to be expected that the relation of tuberculosis to crowded living would be even more strongly emphasized if a study could be added of the number of people per dwelling room as well as population per square mile, for even in the density groups of less than 5000 per square mile, many areas exist where a small crowded urban district is balanced by a sparsely populated surrounding semirural area, producing a low population-density figure for the community, not truly representative of the situation. Even in entirely rural areas, people of low economic level are often crowded together into too few rooms.

It is apparent that the densely populated areas also include more poor tenement districts of low socioeconomic level. Hence, without investigation it is impossible to say that the increase in tuberculosis in the high-population densities is not due so much to their low economic level as to crowding per se.

It is of the greatest importance to differentiate the effect of low socioeconomic level from that of population density. The average desirability level of those communities in the 2000 to 5000 population-density group proved to be C, whereas the desirability level in the highest density group proved to be E. By referring to the previously charted relation of tuberculosis to desirability, the rates to be expected for these two groups on the basis of

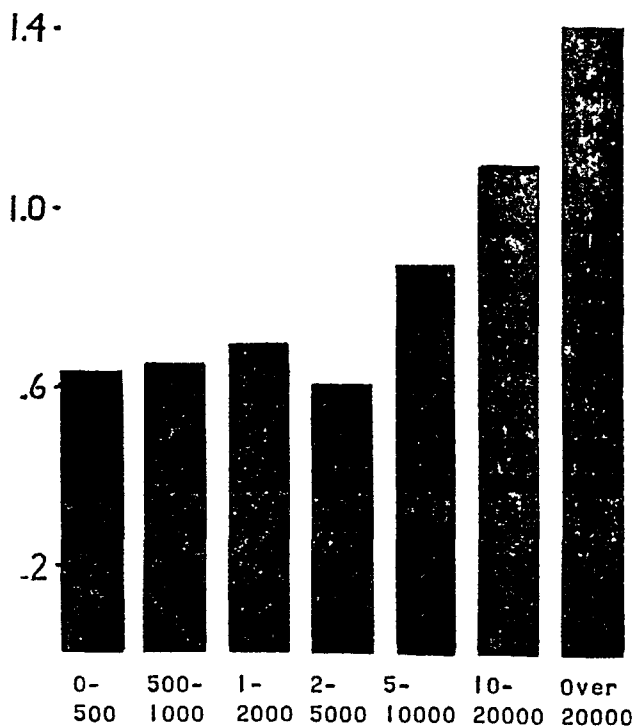


FIGURE 2. Incidence of Pulmonary Tuberculosis in Different Population Densities, Classified according to People per Square Mile.

high incidence here demonstrates that even the best environment is far from good enough, and that efforts must be directed not only at the community of low socioeconomic level but also at the entire range of society. Of the twelve communities in the highest desirability bracket, only one presented an outstandingly high incidence of tuberculosis. Of the eight communities with the lowest desirability rating, only one presented a low incidence.

Tuberculosis Rate and Population Density

As shown in Figure 2, in which all communities are grouped under like population densities, the four least dense groupings, those with densities of less than 5000 per square mile, presented similar averages of tuberculosis incidence. This suggests that insofar as can be determined from this study, population densities up to 5000 per square mile do not exert an unfavorable influence on the rate of pulmonary tuberculosis. Of the forty-six

desirability alone are shown to be 0.8 and 0.9 per cent, respectively. But since the rates that were found on the basis of population density were 0.6 and 1.4 per cent, it can be seen that the factor of population density was largely responsible for the increased prevalence in the crowded areas. Hence, increased population density above a certain level produces more tuberculosis even independently of socioeconomic level.

To distinguish further between the effect of density and that of desirability, the tuberculosis rates for those communities of the same desirability level were plotted against the various population densities of the communities included in each group. Only desirability groups C and D were used, for not enough communities were represented in any one other group to be broken down into a satisfactory variety of population densities. A good correlation was shown of pulmonary tuberculosis rates with population density in communities classified in the same socioeconomic level. Hence, the tuberculosis rates ascend in increased population densities, even independently of the socioeconomic level of the communities considered. On the other hand, the correlation between pulmonary tuberculosis and community desirability in the same population density is poor, but this may be due to the small number of communities in each population-density group rather than to the weakness of the influence of socioeconomic level independent of density that would be suggested.

Although this attempt to distinguish between population density and socioeconomic level is difficult, and the extent of this study is not sufficient for the final evaluation of such an intricate relation, it does suggest strongly that population density in itself is perhaps the most important consideration in the incidence of pulmonary tuberculosis.

Tuberculosis Rate and Community Welfare Rate

Welfare rates based on the period of 1936-1939, as recorded by Lambie,⁷ were used because they were judged to be more representative of the community than would any rate based on the present time. No uniform relation existed throughout the four divisions of welfare rates, but the communities with the highest welfare rates had 1.0 per cent tuberculosis against an average of 0.8 per cent in the communities with lower welfare rates. This is hardly worthy of note, but since it is based on a single purely objective factor, it is considered for the sake of completeness.

Tuberculosis Rate and Community Nationality

Only those communities where a dominant nationality was considered as contributory to

community homogeneity were included in this study, approximately 50 per cent or more being of the same general nationality. Nationality was determined by the birthplace of the subject or his parents in a foreign country. It must be noted that this is not a study of incidence of tuberculosis in persons of different nationalities but in communities of the same nationality.

In each group of communities of the same nationality there was a decided variation between its members, suggesting that nationality does not influence tuberculosis incidence to a sufficient degree to overcome all the other factors in the community that affect this rate. Furthermore, the desirability rating and population density of the community served to explain for the most part any difference in nationality that did exist.

It may be mentioned for completeness, however, that the average percentages of pulmonary tuberculosis for each community group by nationality were as follows: Irish, 1.3 per cent; Jewish, 1.0 per cent; Italian, 0.9 per cent; and Portuguese, 0.6 per cent. The crowded housing and low socioeconomic level of the Irish communities were the likely causative factors, since a consideration of these communities on the basis of a desirability rating of F and a population density greater than 20,000 alone would lead to the same incidence of tuberculosis irrespective of nationality.

The fact that Italian communities all happened to be of very different population density offers an opportunity for comparing incidence of tuberculosis in communities of the same nationality but with different population densities (Table 1).

TABLE 1. *Tuberculosis Incidences in Four Italian Communities Compared to Their Population Densities.*

COMMUNITY	POPULATION DENSITY	No. OF INDICES EXAMINED	INDICES WITH PULMONARY TUBERCULOSIS	
			%	
C 51	60,000	2,408	1.2	
C 21	25,000	2,779	0.9	
C 89	7,000	990	0.7	
C 201	1,500	743	0.4	

From the table it is evident that whatever influence nationality may have on tuberculosis incidence is eclipsed by other factors—in this case, population density.

Tuberculosis Rate and Community Occupation

A consideration similar to that made of nationalities was made of pulmonary tuberculosis by community occupation, considering only those communities wherein a dominant type of occupation was represented. The average rates for communities grouped by each occupation were

as follows: urban office-workers (chiefly employees) 1.1 per cent; fishing, 1.0 per cent; leather and shoe manufacturing, 0.8 per cent; textile manufacturing, 0.6 per cent; suburban office-workers (chiefly employers), 0.6 per cent and farming, 0.4 per cent. There was such a variation in tuberculosis incidence between different communities within the same occupational group that it seems apparent that the community's major occupation itself has little or nothing to do with tuberculosis incidence, insofar as those occupations here considered are concerned. The only occupational group with uniform incidence throughout the several communities constituting the group was that of farming, with the low rate of 0.4 per cent. This is consistent with, although in excess of, the low incidence previously demonstrated in the low population densities, and hence can be partly attributed to decreased contact from uncrowded living. One might go farther and attribute it, in part, to outdoor work and freedom from the stress of urban life.

Although the textile (0.6 per cent) and shoe-manufacturing communities (0.8 per cent) do not form homogeneous groups, the fact that their average rates for tuberculosis are below the general average is worthy of note, since some authors have considered that industrial communities have a very high tuberculosis rate.

Comparison of Communities with Highest and Lowest Tuberculosis Rates

The one hundred and thirteen communities sending registrants to this induction station were listed in rank order according to the incidence of pulmonary tuberculosis found in selectees from each. The range covered was from the high rate of 2.4 per cent found in the most crowded area under consideration, composed of Italian and a mixed foreign population including Chinese, to 0.05 per cent in a small jewelry-manufacturing city with an outlying area devoted to farming, composed mainly of an old-line native population with a small mixed foreign element.

A comparison was made of the seventeen communities with the highest tuberculosis incidence with the seventeen with the lowest incidence to check the previous findings and if possible to furnish information on the socioeconomic aspects of pulmonary tuberculosis. Of the seventeen communities with the highest tuberculosis rates, eleven were of high population density with a low socioeconomic level. Of the seventeen communities with the lowest tuberculosis rates, twelve were of low population density with moderate or high desirability.

In a comparison of nationalities, eleven of the seventeen communities with a high incidence of

tuberculosis contained a major element of population of foreign birth or first-generation American born, whereas the same foreign element was predominant in only six of the seventeen communities with the lowest incidence of tuberculosis. No community with the lowest desirability rating and only one with high population density was represented among the communities with a low tuberculosis rate.

A comparison of the size of the cities in the two groups is interesting, for none of the communities with a low incidence of tuberculosis were in Boston, whereas thirteen of the seventeen communities with the highest incidence were in that city.

SUMMARY

Of the selectees examined at the Boston Armed Forces Induction Station from December, 1940, to early in 1943, 0.9 per cent were found by x-ray examination to have pulmonary tuberculosis.

There was progressively more pulmonary tuberculosis in selectees from communities of low socioeconomic level than in those from the better communities, with 1.4 per cent in the poorest and 0.7 per cent in the best communities.

The incidence of pulmonary tuberculosis was uninfluenced by variations in population densities under 5000 per square mile, but in greater densities it increased progressively from 0.6 per cent at population densities of 5000 to 1.4 per cent at population densities of over 20,000 per square mile.

The association of a higher rate of tuberculosis with the higher densities of population appears to be due to population density per se and not merely to the lower socioeconomic level of the congested areas. There is some evidence that the effect of socioeconomic level is secondary to population density.

The correlation of tuberculosis death rates of five years, 1937-1941, with both community socioeconomic level and population density gave results similar to those of the correlation of tuberculosis incidence, showing the close relation of morbidity and mortality studies of this disease.

Of communities with a dominant nationality the Irish communities presented the highest tuberculosis rates, with an average of 1.3 per cent. This incidence was no greater than would be expected on the basis of their high population density and low desirability irrespective of nationality. The tuberculosis rates in Italian communities varied with population density; hence, nationality was not shown to be a factor in the incidence of pulmonary tuberculosis.

No specific relation between community occupation and tuberculosis could be found. In the

trial communities presented average and below-average rates. Farming communities had the least tuberculosis—an incidence of 0.4 per cent.

This study of tuberculosis on a community socioeconomic basis points to a sufficiently close relation between tuberculosis incidence and both population density and socioeconomic level to demonstrate the need for future extensive investigation of these factors.

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MEDICAL PROGRESS

THE TREATMENT OF THERMAL BURNS

I. General Outline

NATIONAL RESEARCH COUNCIL*

WASHINGTON, D. C.

THE treatment of thermal burns is one of the most acute problems of war surgery; it has been the subject of many publications, and many discussions have been devoted to it. The abundance of details and the frequently contradictory character of the evidence, however, sometimes make it difficult to see the main trends of the development. For this reason, the present general outline sketched on a historical background has been prepared. It goes back to the introduction of the tannic acid treatment by Davidson in 1925, without, however, in any way attempting to be exhaustive or to provide a comprehensive bibliography of the subject. The existing monographs by Pack and Davis, Hilgenfeldt, and Harkins, as well as Volume V of *Military Surgical Manuals*, entitled *Burns, Shock, Wound Healing and Vascular Injuries*, which has just been published, make such an undertaking unnecessary. It should be noted, moreover, that in preparing this outline abstracts published in the *Bulletin of War Medicine* and in *War Medicine* were often relied on.

PREWAR PERIOD

For many centuries the chief aim in the treatment of burns was the promotion of good healing. Consciously or unconsciously, this included the prevention of dangerous sepsis. It was no-

ticed, moreover, that the blood of patients suffering from burns often showed increased viscosity, and the infusion of saline solutions had become popular before World War I.¹ But on the whole, the treatment was local and very often purely empirical. From the time of Hippocrates, a host of drugs has been applied, and the so-called "Hippocratic Collection" itself lists several prescriptions, one of them employing oak root (*Quercus ilex*), which supposedly contains tannic acid and may have had an astringent or even tanning effect.²

In the course of World War I and its aftermath, increasing attention was paid to the phenomenon of shock. Burns presented themselves more clearly as a thermal trauma that was often followed by shock, was easily open to infection, and might lead to disfiguring scars and contractures. The pathology and treatment of burns, therefore, became special problems in such wider surgical provinces as shock, wound infection and plastic surgery.

These various aspects are reflected in the classification of burns. The classic grouping since Dupuytren³ was a histologic one—that is, according to the depth of skin involved.³ His distinction of six degrees proved, however, less practical than a classification into three degrees. The latter might be based on the clinical aspects—that is, erythema, blistering and charring³—or on a direct appraisal of the layers destroyed—that is, superficial destruction, deep destruction and

*The articles in the medical progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III. 678 pp. Spring 1941. Illinois: Charles C. Thomas, 1941. \$5.00).

*Prepared by the Office of Medical Information and released under the date of February 17, 1943.

complete destruction of skin.³ Apart from expressing the severity of the burn, it also made it possible to distinguish between burns where the skin would regenerate and those where skin grafting was required. Later on this point of view was even more strongly emphasized by Hall, Cade and McIndoe who proposed a distinction between "partial skin loss" (first and second degrees) and "complete skin loss" (third degree).³

Since, however, the severity of a burn and the extent of the subsequent shock were even more dependent on the extent of the burned area, an estimate of the latter was of prime importance. Such an estimate was provided by the Berkow⁴ method in 1924. The general attention this scheme has received and its usefulness for the estimate of plasma protein loss and plasma transfusion required,⁵ are in themselves a testimony to the increasing emphasis laid on shock.

Likewise, it was the problem of shock that in 1925 led Davidson⁶ to the introduction of the tannic acid treatment of burns. Reviewing the various explanations of the clinical picture commonly described by such a term as "shock" or "exhaustion," Davidson concluded that the constitutional reaction is probably due to absorption of some toxic substance or substances from the burned area. Such absorption, he thought, might be prevented, and he chose tannic acid to precipitate the poisonous materials in burned tissue. It is interesting to note that Davidson was also influenced by the work of Bardeen,⁷ who in 1898 had observed damage of the liver and other organs following burns.

Although the precipitation of toxic substances was the key point for Davidson, he believed that the treatment had several additional advantages. He emphasized the analgesic effect, the minimal trauma and general comfort of the patient, the prevention of loss of body fluid, the limitation of secondary infection, the less marked scar-tissue formation and the scaffold offered for the growth of young epithelial cells.

The fact that Davidson considered the prevention of loss of body fluid forms a link between his work and that of Underhill.⁸ While engaged in the study of poisoning by war gases, particularly phosgene, during the last war, Underhill paid increasing attention to changes in blood concentration. Extending his studies to the problem of burns, he was later on followed by Blalock and others.^{1,9} These workers elaborated a theory of burn shock as a result of injury to the capillaries, anhydremia, fluid shift and anoxia. It was, moreover, shown that the fluid shifting toward the burned area had the character of blood plasma, and that the circulating blood was relatively

rich in blood corpuscles but poor in plasma proteins. These results had in the main been arrived at before the outbreak of the present war, but many points are still disputed. The process as it is now usually pictured has, however, been summed up as follows: "The local thermal trauma produces a local capillary injury with regional loss of plasma-like fluid both into the burned tissues and from the skin by means of 'weeping.' Later there may be generalized infiltration of plasma into tissues remote from the region of the burn. The quantitative aspect of the loss of plasma is of especial significance; the loss may exceed several liters."⁵

Although this theory of shock differed widely from Davidson's ideas, it did not oppose the tannic acid treatment. It had become doubtful whether tannic acid acted by precipitating toxic agents, but as Blalock¹⁰ stated in 1931, "It is entirely possible that such agencies as tannic acid and epinephrin exert their beneficial effects by preventing loss of fluid rather than by stopping the absorption of toxins."

An attack on the theory of toxemia and the use of tannic acid came from a different direction. Aldrich,¹¹ in 1933, denied the existence of non-bacterial toxemia in burns; in his opinion the toxemia was due to sepsis. His view ran parallel to the observation that in many cases where coagulation with tannic acid had been practiced, infection had developed underneath the eschar. Bancroft and Rogers,¹² who had remarked on the latter fact as early as 1928, had adopted—for certain cases, at least—the treatment with acriflavine. Aldrich employed gentian violet, the bactericidal and bacteriostatic properties of which had been made known by Churchman¹³ in 1912, for the treatment of burns, claiming that it was particularly effective in combating *Streptococcus hemolyticus*. Subsequently, Aldrich¹⁴ used triple dye—that is, a mixture of brilliant green and acriviolet (acriflavine and crystal violet). Brilliant green had been in use as an antiseptic for quite a number of years, and in a 1 per cent solution Koritkin-Nowikow had employed it for burns and scalds in 1934.¹

Other criticisms voiced before the present war against the use (or sole use) of tannic acid may be mentioned. Bettman,¹⁵ in treating an extensive burn of the arm of a five-month-old child, had observed a progressively increasing edema with subsequent pressure and impediment of the circulation that led to a sloughing of the hand. In order to obviate the slowness of tanning and the rigidity of the eschar by tannic acid, he preferred the tannic acid-silver nitrate method that he had proposed in 1935. Here again a much older thera-

peutic agent had been reintroduced in a new combination, silver nitrate having been used in burns as early as 1858 by Kalt.¹

In Germany, Löhr, in 1934, introduced the cod-liver oil treatment of burns.¹⁰ He pointed out that tannic acid did not prevent shock and sometimes led to infections under the scab. Cod-liver oil, which he used in the form of *Unguentolan*,—that is, mixed with other ointments,—prevented infections and helped the healing of the burns. Taylor in 1936 remarked that tannic acid hindered the growth of epithelium.⁹

Under this two-sided assault the existence of toxemia due to burns became questionable. In 1938, Wilson, MacGregor and Stewart¹⁷ wrote: "The present trend of opinion seems to be towards Underhill's view that increased concentration of the blood is the main, even the sole, cause of symptoms in the stage of toxæmia; some support, however, is given to Aldrich's belief in the predominating influence of hemolytic streptococcus infection. An attitude of scepticism or reserve towards a specific burn toxin has become fashionable."

But Wilson and his co-workers thought that they could prove the existence of a separate stage of acute toxemia as distinguished from shock on the one hand and septic toxemia on the other. They differentiated five stages in the course of burns: initial shock (the first two hours after the burn); secondary shock (two or more hours after injury); acute toxemia (six to fifty hours after injury); septic toxemia (approximately from the fourth day on); and healing. The stage of acute toxemia, in their opinion, was marked not only by clinical symptoms but by liver damage as well. Although they used tannic acid, which has recently been found to have a toxic effect of its own, they believed that the liver lesion furnished the strongest indication of a nonbacterial toxin circulating during the first few days after a burn.

This outline of the possible course of a severe burn has become the basis for much subsequent discussion. As will be seen later, their evidence for the existence of nonbacterial toxemia has lost much of its strength, although the question has not yet been finally decided. At the time, however, it gave renewed impetus to the belief in a toxic agent.¹⁸ Moreover, it vindicated the original rationale for the use of tannic acid, if indeed such a vindication was necessary. For in spite of the criticism by Aldrich and a few others, tannic acid, possibly in combination with silver nitrate or antiseptics, remained the local medication of choice for the hospital treatment of burns. Besides, chemotherapy in the form of sulfonamide drugs used orally or locally had come into use. Here, then, was a new, powerful remedy to ob-

viate the danger of sepsis that tannic acid alone might not always prevent.

PERIOD FROM OUTBREAK OF WAR UNTIL PEARL HARBOR

At the outbreak of war, the treatment of burns was relatively uniform. In first-aid treatment, picric acid was given preference in Great Britain as well as in this country. *The Memorandum for the Guidance of Medical Officers and Other Personnel at First Aid Posts* of the British Emergency Medical Services,¹⁹ issued in 1939, states: "No attempt should be made at cleaning these [burns]. They should simply be covered with a suitable dressing. The burn dressing (picric acid) should be moistened before application. Picric acid does not interfere with the efficiency of tannic acid dressing applied later. Morphia will probably be required." The American Red Cross *First Aid Textbook*,²⁰ similarly placed picric acid first, and so did the War Department field manual, *Military Sanitation and First Aid*,²¹ published in 1940, although in the two latter publications tannic acid was given an almost equal place. Due stress was placed on combating shock by keeping the patient warm and providing him with fluids.

In the hospital, treatment with tannic acid alone or in combination with silver nitrate or antiseptics predominated. An example is the procedure recommended by McClure,¹⁸ of the Henry Ford Hospital, Detroit. Measures to control shock came first. The patient was given sedatives, heat externally, fluids (5 per cent dextrose and a physiologic solution of sodium chloride) and transfusions of blood plasma. The local treatment consisted in removing the clothing, superficial débridement and application of a 5 per cent freshly prepared solution of tannic acid with an atomizer or power spray. Collections of pus under the tan were liberated, skin grafting was employed early, and blood transfusions were given in late stages of secondary anemia. McClure emphasized the need for strict aseptic precautions during the surgical procedures, since the burned area should be regarded as a large open surgical wound.

This method represented one of the most advanced patterns of treatment, particularly as regards assepsis, which was too often neglected in routine practice. Other surgeons preferred silver nitrate in combination with the tannic acid or the addition of resorcinol. Still others painted the edges of the tan with antiseptics.²² It must also be remembered that gentian violet and triple dye had their advocates, but on the whole, coagulation with tannic acid in one form or another was the treatment of choice.

Before entering on the changes brought about by the experience of the war, two points that

later on became important in the treatment of shock should be mentioned. Early in 1940, Elkinton, Wolff and Lee²³ showed that the restoration of lost plasma proteins depends on the time when capillary impermeability is restored and on the amount of protein needed. In their opinion, loss of plasma continues for thirty to forty hours, and during this time repeated small plasma transfusions will prevent hemoconcentration. After forty hours a large plasma transfusion is given to make up the plasma deficit. They also proposed a formula for calculating the deficit, and various other methods for calculation were suggested by other authors.⁵ The work of Elkinton and his associates made it particularly clear that transfusions had to be given in the very early period after the injury. Estimates of the amount of plasma required, based on the extent of the burn, on hematocrit and hemoglobin readings and on calculations of the plasma deficit, assumed an important place in subsequent outlines of the treatment of burns.⁵ The quest for plasma and serum substitutes, on the other hand, did not meet with unequivocal success.²⁴ Secondly, it was realized that the administration of saline solutions was dangerous since it tended to increase the edema²⁵—unless vomiting had led to a serious loss of chlorides.³

In anticipating these points it can be shown that the general treatment of shock followed a gradual development. Although many theoretical points remain debatable, no completely new aspects have been introduced during the war,* as in the case of the local treatment.

The fall of France, the evacuation of Dunkirk and the subsequent battle of Britain changed the perspective as well as many details of the treatment of burns. The British soldiers returning from France, the personnel of the R.A.F. and the civilians bombed in the British Isles suffered heavily from burns. From the spring of 1940 until the spring of the following year, the British had to cope with new and unforeseen conditions. Large numbers of burned persons had to be treated at first-aid posts or under first-aid conditions, treatment on board ship also falling into this category.^{28, 29} Often considerable time passed before patients were transferred to the hospitals, where facilities were overtaxed and work had to be performed under most difficult circumstances. Under the impact of the emergency, the need for certain adjustments made itself felt. Cohen,³⁰ who treated men evacuated from Dunkirk in a hospital of the Emergency Medical Service, remarked, "Many lessons were gathered, but one lesson stood

out clearly from it all—the necessity for and the value of a prepared routine of treatment [in hospitals]." The demands on doctors, nurses and hospital facilities were so heavy that makeshift arrangements were quite inadequate. Again and again in following years, the need for co-operating teams, including experienced general surgeons, plastic surgeons and even pathologists, as well as the desirability of burn centers, has been stressed.^{31, 32} Only recently, the disadvantages of lack of prepared routine were demonstrated when a fire broke out in a Knights of Columbus leave center in St. Johns, Newfoundland.³³ Seventy-seven patients had to be taken to various hospitals that, as can easily be understood, were not adequately prepared for such a disaster. As a result, many necessary materials were lacking and many different forms of treatment were employed by the staffs of the various hospitals.

Another lesson that was learned in Britain was the need for proper instruction of first-aid personnel. It was necessary to distinguish between those cases that might receive preliminary or definitive treatment by first-aiders and those that had to be transported to a hospital as soon as possible. This led to an increasing emphasis on a short, practical classification, as for instance into "minor" and "major" burns.³⁴ Regarding the latter class, it also led to restrictions in the local first-aid treatment, that many authorities kept to an absolute minimum, simply covering a severely burned part with clean towels, cloth or *tulle gras* or first powdering them with sulfanilamide.³⁴ Still others consented to more active measures, particularly if transport was delayed, as for instance in naval action.^{32, 34} The instructions of Emergency Medical Services,³⁵ dated June, 1941, advise: "*Serious burns* requiring admission to hospital should be treated by the application of sterile vaseline on gauze or lint to cover the exposed portions of the burn. Provided the patient is shortly to be transferred to a nearby hospital, no attempt should be made to remove clothing in order to expose the entire burn area. Serious burns always require injections of morphine for pain, in full doses ($\frac{1}{3}$ to $\frac{1}{2}$ gr. for adults)."

Although the points mentioned so far chiefly concerned organization and instruction for the treatment of burns, the very soundness of the prewar local treatment began to be questioned. To meet the danger of contractures under tannic acid treatment, the extremities, particularly the fingers, had been splinted³⁶ or extension apparatus used,¹⁸ but such measures were not sufficient. The fact that a great many war burns had affected the face and hands led to an early recommendation to substitute saline packs or baths on

*Recent research has made the traditional therapy of shock by external heat questionable, and it has also detracted from the value of oxygen inhalations.^{26, 27} These new aspects, however, have as yet hardly made an impact on the treatment of burns.

the so-called "critical areas." This recommendation did not, however, meet with general approval,³⁷ particularly since it was understood as a general rejection of the tannic acid treatment altogether. Whereas the majority of physicians followed the new directions and avoided tannic acid on the face and the hands, others defended the treatment and stated either that its condemnation was not at all justified or that there was not yet sufficient evidence for the rejection. A conference on the treatment of war wounds, organized by the War Wounds Committee of the British Medical Research Council on November 29, 1940, showed how vigorous was the defense.³⁸⁻⁴¹ Finally, there was a third group⁴² that tended to avoid tannic acid altogether.

Reviewing briefly the discussion for and against tannic acid treatment, the following trend is apparent. Those defending it pointed to the decrease in the mortality rate following the introduction of tannic acid. They maintained that the saving of life held precedence over the saving of function.⁴³⁻⁴¹ The opposition largely argued on the basis of the Hippocratic principle, *Nil nocere*. Saline baths and packs, which were so favorably received in Great Britain, owed some of their popularity to the advantages they offered to early skin grafting.⁴⁵ Most authorities agreed on the following point: burns that did not epithelialize promptly needed grafting, and sepsis was one of the major obstacles to the early performance of this operation. But among those who stressed the deleterious effects of sepsis were also advocates of triple dye therapy,³² which, as has been seen, had been devised for the prevention of infection.

Besides the use of saline baths, silver nitrate, triple dye, gentian violet and other drugs already mentioned, there emerged a host of different therapeutic procedures. The use of trypsin to clear up the burned surface was envisaged,³⁸ Euglamide⁴⁶ and the closed plaster treatment⁴⁷ were recommended, and Bunyan,⁴⁸⁻⁴⁹ followed by other workers, suggested the envelope method with irrigations.* The latter method was recently illustrated in a popular American magazine,⁵¹ after Biodyne ointment had also received publicity.⁵² These are but a few items from a long list.⁵³ By the middle of 1941, the local treatment of burns had become so confused that even the reintroduction of the much abused carron oil seemed possible, and anything might be good if, in addition, sulfonamide drugs were prescribed.⁵⁴⁻⁵⁵

The local application of sulfonamide, which at the outbreak of the war appeared to have great

promise, also had its ups and downs. Omitted by some⁴⁰ and cautiously used over small areas, usually in combination with coagulants, by others,⁵⁶ it was employed by still others as *the* local treatment. Best known among the latter methods was the one announced in August, 1941, by Pickrell,⁵⁷ who sprayed the burned area with 3 per cent sulfadiazine in 8 per cent triethanolamine. The Pickrell method was criticized by H. S. Allen and Koch,⁵⁸ who, however, conceded that sulfathiazole ointment, introduced by J. G. Allen, Owens and others⁵⁹ in May, 1942, might be useful in first aid. In Canada, Skinner and Waud⁶⁰ were working with plastic films of polyvinyl alcohol containing sulfonamide drugs. Among the other local applications of these drugs mentioned in the literature hydrated films containing 10 per cent sulfanilamide and buffer, with and without quantities of azochloramide,⁶¹⁻⁶² may be cited as one of the most recent proposals.

PERIOD AFTER PEARL HARBOR

The disaster at Pearl Harbor on December 7, 1941, resulted in a great number of burns, and the treatment given shows some decisive differences as compared with the British procedure in 1940. Whereas in Great Britain shock had been mainly combated by keeping the patients warm and giving them large quantities of fluids orally at Pearl Harbor, in addition, blood plasma, supplemented by glucose and saline solution, was used in most cases. The local medication too varied considerably, at the United States Naval Hospital, for instance, it included sulfanilamide powder, sulfanilamide in mineral oil spray, sulfathiazole suspension, gentian violet spray and boric acid wet dressings.⁶³ At the dispensary of the Naval Air Station, on the other hand, the treatment was divided between tannic acid and sulfonamides.⁶⁴

But in spite of all the criticism and the many alternative remedies suggested, coagulation with tannic acid still predominated in the first half of 1942. In England, it is true, it had been removed from the schedule of first aid posts by March, 1942 and dressings of soft paraffin ointment had been advised instead.⁶⁵ It had also generally been recognized by this time that tannic acid should not be used on critical areas. For the rest, the state of affairs is approximately characterized by the recommendations of the National Research Council formulated in January, 1942.⁶⁶ Regarding first aid treatment it is here stated: "All burned surfaces except the face, hands and genitalia should be liberally coated with a water soluble jelly containing 10 per cent tannic acid and 5 per cent sulfadiazine. Burns of the face, hands and gen-

*Kilner recently advocated the first aid Bunyan bag filled with sulfonamide.⁵⁰

italia should be covered with a water-soluble emulsion containing 5 per cent of sulfadiazine." The definitive treatment of other areas envisaged tannic acid, 10 per cent, and silver nitrate, 10 per cent. Sulfadiazine was given orally as a routine measure. These recommendations of the National Research Council are echoed in the booklet of the Office of Civilian Defense⁶⁷ and represent opinions also found in the *Guides to Therapy* of the War Department⁶⁸ and in other publications of the time. *Treatment of Thermal Burns* issued by the National Research Council of Canada³ on August 6, 1942, although much more detailed regarding the pathology as well as the treatment of burns, also makes recommendations that are in basic agreement with those of the American National Research Council. In spite of all criticisms, qualifications and alternatives suggested, tannic acid by the middle of last year had not been superseded by any other single medication.

The recommendations of the research councils of the United States and Canada mention a point that indicates the further development. For burns on the hands, they suggest a firm-pressure bandage. This was an early recognition of a method that was soon to have a much wider application. Impressed by the inconclusive search for a burn toxin, some American physicians proposed to regard a burn simply as a large, open wound.⁶⁹ From this principle they deduced a simple technic. The burned area had to be examined, cleansed, and covered under strictly aseptic safeguards. The covering had to be nonirritant and had to protect the surface and prevent loss of fluid. "A large pressure dressing similar to that applied over skin graft seems to be advantageous in that it helps to immobilize the part and minimize the loss of fluid into the tissues about the burn." From January 1, 1939, on, the mortality rate at the Cook County Hospital in Chicago was considerably reduced by thorough cleansing and a pressure dressing over vaseline gauze. This treatment, first detailed for burns of the hand,⁷⁰ became more widely known through a paper by Allen and Koch⁶⁸ concerning the treatment of patients with severe burns.

Discarding the existence of burn toxins, Allen and Koch still had to account for the liver damage in certain cases. They attributed it to the use of general anesthesia, the danger of which, particularly in patients suffering from shock, had also been pointed out by others.³ But it was just the existence of liver necrosis, used as evidence for burn toxemia by Wilson, that led to a much more decisive argument against tannic acid than any advanced before. The studies by Wilson and his co-workers had been followed up by other observers. In April, 1941, Buis and Hartman⁷¹ found

that shock with plasma loss and hemoconcentration occurs in experimental burns and produces acute congestion of the tissues, especially the liver. Without excluding the possible existence of a burn toxin, they suggested that anoxia resulted from the shock, plasma loss, hemoconcentration and acute congestion as contributing causes of the liver necrosis. But a few months later Wells, Humphrey and Coll,⁷² at a meeting of the New England Surgical Society, gave a different interpretation of the liver damage. They claimed that the central necrosis of the liver was the result of treatment with tannic acid solution, tannic acid jelly or tannic acid and silver nitrate solutions. The dangers of the tannic acid treatment in turn enhanced the advantages of the Koch method, both being brought to the attention of a wider public in an editorial published in May, 1942, in the *Journal of the American Medical Association*.⁷³

Studies by Siler and Reid⁷⁴ presented experimental evidence suggesting that primary pressure dressings may reduce the loss of plasma at the site of, and into the surrounding tissues of, burned areas. On the other hand, the practical possibilities of the pressure method, which presupposes the strictest aseptic technic, were regarded with some skepticism by the armed forces. At the present moment, it cannot be said that any single method has been accepted to the exclusion of all others. The local treatment chosen depends on the site of the burn as well as on its degree, and Volume V of the *Military Surgical Manuals*⁷⁵ lists a considerable variety of medications including tannic acid, sulfonamide drugs, saline baths, boric ointment, the Bunyan-Stannard envelope and triple dye, as well as the pressure dressing. But the last-named method stands in the foreground of the debate. At the Coconut Grove fire on November 28, 1942, it underwent a favorable test,⁷⁶ and is now recommended by the National Research Council. In *Circular Letter No. 15*, dated January 11, 1943, from the Surgeon General's Office,⁷⁷ the treatment of burns with boric acid ointment is given first place, and the importance of firm pressure is stressed, especially in burns of the hands and face.

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Stated Meeting, October 6, 1943

A STATED meeting of the Council of the Massachusetts Medical Society was called to order by the president, Dr. Roger I. Lee, Suffolk, in John Ware Hall, 8 Fenway, Boston, at 10:00 a.m., on Wednesday, October 6, 1943. There were 215 councilors present (Appendix No. 1).

On a motion by Dr. Reginald Fitz, Suffolk, and a second by Dr. David Cheever, Suffolk, the record of the last meeting of the Council (May 24, 1943), as published in the *New England Journal of Medicine*, issue of July 8, 1943, was approved.

Dr. Lee, in commenting on the death of Dr. Halbert G. Stetson, spoke as follows:

It is the sad duty of the President to announce that Dr. Halbert G. Stetson, of Greenfield, a former president of the Massachusetts Medical Society, died on September 15, 1943. Dr. Stetson was probably known to everybody in the room. He was in his seventy-sixth year.

He received his degree in medicine from the College of Physicians and Surgeons of Baltimore in 1895.

Dr. Stetson had been a prominent member of the Massachusetts Medical Society, giving freely of his time and energy to his activities. He was president of the Society from 1931-1933. He was a delegate from the Massachusetts Medical Society to the House of Delegates of the American Medical Association for twenty years—1912-1932. He had been a member of the Council for many years. He likewise served as nominating councilor for many years. He was a member of the Committee on Public Relations from 1935 to 1943. He was president of the Franklin District Medical Society from 1901-1903. He also served as secretary-treasurer of this district society for many years.

From 1921 to his death he served as medical examiner for the Eastern District of Franklin County.

He had served as chairman of the Greenfield school board and president of the Franklin County Public Hospital Corporation. He was formerly president of the New York and New England Association of Railway Surgeons and the Connecticut Valley Medical Association.

Dr. Stetson was a member of the Scientific Assembly of the American Medical Association.

It was moved by Dr. Walter G. Phippen, Essex South, and seconded by Dr. Cheever that this memorial be placed upon the records. It was so ordered by vote of the Council.

REPORT OF EXECUTIVE COMMITTEE

The Secretary reported as follows:

The Executive Committee of the Council, at its meeting held on August 25, 1943, discussed the advisability of calling a conference of those who might be expected to represent the point of view of the ma-

jority of the physicians of New England anent the Wagner-Murray-Dingell Bill.

It was voted by the committee to empower the president, Dr. Roger I. Lee, to appoint a committee looking toward this end. Pursuant to this action, the following committee was appointed by Dr. Lee: Dr. Walter G. Phippen, chairman, Dr. Frank R. Ober, Dr. Brainard F. Conley and Dr. Michael A. Tighe. This committee will report its activities later in this meeting.

The committee regarded this matter as an emergency inasmuch as Congress was to reconvene in a few days and inasmuch as the committee was given to understand that hearings on this bill were to begin immediately after the Congressional recess.

(The Secretary moved that the Council approve this action of the Executive Committee. This motion was seconded by a councilor and it was so ordered by vote of the Council.)

The committee reviewed the reports of the following committees: Membership, Postwar Loan Fund, Public Relations and War Participation, and approved of their respective recommendations.

In relation to that part of the report of the Committee on Public Relations that deals with the operation in Massachusetts of the plan of the Children's Bureau for the maternity care of wives and infants of enlisted men, the committee expressed its approval in principle and so notified Dr. Vlado A. Getting, Massachusetts commissioner of public health. The Council has received advance information on this matter.

The War Participation Committee, under a directive of the Council, studied a plan organized by the staff of the Beth Israel Hospital for the care of the patients of those of their members who had entered the various services of the United States. In this directive the Council ordered the War Participation Committee to report on the matter to the Executive Committee of the Council.

In accordance with the recommendation of the War Participation Committee, the Executive Committee expresses its sympathy with the ideology involved but does not recommend approval by the Society of the plan as outlined in the protocol.

(The Secretary moved the adoption of this recommendation. This motion was seconded by a councilor. Dr. George L. Schadt, Hampden, asked if, by the Secretary's motion, the Council was being asked to approve the administrative setup in Massachusetts of the plan of the Children's Bureau for the maternal and infant care of soldiers' dependents. The Secretary replied that the Committee was offering no motion with regard to this plan and that the debate on this particular matter would come when the report of the Committee on Public Relations was offered. The motion before the house, he continued, had to do with the plan of the staff of the Beth Israel Hospital for the care of the patients of those of their members who had entered the United States service. The motion was adopted by vote of the Council.)

The Committee, under a directive of the Council, reconsidered the matter of sending gratis one hundred subscriptions of the *New England Journal of Medicine* for one year to the United States Navy and now so recommends

(The Secretary moved the adoption of this recommendation. This motion was seconded by a councilor. Dr. Carl Bearse, Norfolk, expressed the fear that if this recommendation were adopted we would be put in the position of being partial to the Navy. He said that the Army had agreed to buy about six hundred subscriptions. If the Navy were to get these subscriptions free so should the Army. Dr. Richard M. Smith, Suffolk, favored the recommendation because he thought that it would be to the advantage of the *Journal* and that this organ would not particularly suffer because of the expense involved. The motion was adopted by vote of the Council.)

The bylaws of the Massachusetts Medical Service Corporation require that the board of directors of that organization be approved by the Massachusetts Medical Society, which means the Council. The committee was in receipt of a communication from Mr. Twomey, clerk of the Massachusetts Medical Service Corporation, urging an amendment to these bylaws whereby this approval may be given by the Executive Committee of the Council in the name of the Massachusetts Medical Society. This amendment is urged as a matter of convenience, and is approved by the committee.

(The Secretary moved the adoption of this recommendation. This motion was seconded by Dr. Fitz, and it was so ordered by vote of the Council.)

The committee acknowledges the receipt of two letters addressed to the Secretary—one from Dr. Stephen Rushmore, dean of Middlesex University Medical School and the other from Mr. Samuel H. Wragg, president of this university. These letters in substance ask the help of the Massachusetts Medical Society in obtaining clinical teaching facilities for this Medical School. The committee took no action on these letters.

The committee approved certain ad interim appointments made by the President. Dr. Lee will ask for the approval of these appointments later in this meeting.

(The Secretary moved the adoption of this report as a whole. This motion was seconded by a councilor. Dr. Hyman Morrison, Norfolk, asked why the committee did not take any action on the letters of Dr. Rushmore and Mr. Wragg. At the direction of the President the Secretary replied that he could answer the question only from the standpoint of the discussion and debate that took place in the committee when this matter was presented to it. This debate seemed to indicate that it was the feeling of the majority of the committee that the granting of requests contained in these letters would involve the Massachusetts Medical Society in a type of activity in which it should not engage. Dr. Morrison expressed the thought that he had no intention of advocating substandard medical education. He felt, however, that there is an honest effort in this case to improve the teaching and make the school a standard school. He added that he felt that it is along the tradition of the Massachusetts Medical Society to aid this effort. Dr. Harold L. Musgrave, Suffolk, announced that he was a member of the Board of Trustees of Middlesex University Medical School, that this board had been reorganized

and that it now was made up of honest men who were trying to do a good job. He said that the preclinical needs of the school had been vastly improved. The inability to meet clinical needs of the school, however, results in failure in an important way. He added that the two letters spoken of in the report of the Executive Committee were prompted by the fact that a committee was appointed by the Society seven or eight years ago to help the school. He pointed out that the school was no longer a proprietary school and that the real motive behind the letters was an appeal for advisory counsel and nothing more. Dr. Musgrave was advised by the President that any motion which he might have in mind in this matter would more properly come under the heading of new business. The report of the Executive Committee as a whole was adopted by vote of the Council.)

REPORTS OF COMMITTEES

Committee on Publications—Dr. Richard M. Smith, Suffolk, chairman

This report, which is as follows, was offered by Dr. Smith:

The committee has secured Dr. Alfred Blalock, professor of surgery at Johns Hopkins University School of Medicine and surgeon in chief at the Johns Hopkins Hospital, Baltimore, to deliver the Shattuck Lecture at the annual meeting of the Society in 1944.

There are no important matters in connection with the supervision of the publication of the *New England Journal of Medicine* that need to be brought to the attention of the Council at this time. A full report will be made at the February meeting of the Council.

Dr. Smith moved the adoption of the report. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Committee on Arrangements—Dr. Gordon M. Morrison, Middlesex South, chairman

Dr. Roy J. Heffernan, Norfolk, reported for the committee as follows:

Last year your committee looked forward to the 1943 meeting of the Society with some uncertainty. Owing to the absence of so many members in the service, to gasoline restrictions and to other wartime conditions we anticipated a small meeting. Fortunately our fears were groundless: the attendance was only slightly less than the previous year, and the presence of a great number of Army and Navy medical officers made us feel that the meeting was justified. At the present time, the treasurer's books show a profit from that meeting of \$1863.42.

Your committee has voted that the 1944 annual meeting of the Society be held at the Hotel Stadler, Boston, on Tuesday and Wednesday, May 23 and 24, 1944, and that the annual meeting of the Council be held at the same place on Monday evening, May 22, 1944.

Dr. Heffernan moved that the report be accepted. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Ethics and Discipline—Dr. Ralph R. Stratton, Middlesex East, chairman.

The report (Appendix No. 2), which was offered by Dr. Stratton, spoke of two all-day meetings that the committee had held. Many of the cases coming before the committee were of minor importance and were settled by letter. Many others required the committee to conduct hearings.

Many of the complaints had to do with the fees charged by doctors. The committee believes that ordinarily it is not within its province to be involved in disputes of this kind.

The report spoke of three specific cases. One concerned an attempt on the part of a member to injure the professional reputation of certain of his professional brethren. The proof was insufficient and the matter was placed on file. The second case concerned a member who was charged with an active attempt to belittle the professional reputation of two other members. The charge in this case was substantiated and the member in question was asked to resign, which he did. The third case was concerned with the personal conduct of a member who was warned by the committee that his habits must improve.

Dr. Stratton moved the acceptance of this report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Medical Education—Dr. Robert T. Monroe, Norfolk, chairman.

No report.

Committee on Membership—Dr. Harlan F. Newton, Suffolk, chairman.

This report, which was presented by Dr. Newton, is as follows:

The Committee on Membership, meeting with the supervising censors and the Committee on Ethics and Discipline, recommends that the application for reinstatement of Dr. Anthony P. Carogana, of 672 Broadway, Chelsea, this former fellow's resignation having been requested by the Committee on Ethics and Discipline, under the provisions of Chapter I, Section 11, of the by-laws, be approved.

Dr. Newton moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Public Health—Dr. Francis P. Denny, Norfolk, chairman.

No report.

Committee on Medical Defense—Dr. Arthur W. Allen, Suffolk, chairman.

No report.

Committee on Society Headquarters—Dr. William H. Robey, Suffolk, chairman.

No response.

Committee on Finance—Dr. Francis C. Hall, Suffolk, chairman.

No report.

Committee on Industrial Health—Dr. Dwight O'Hara, Middlesex South, chairman.

No response.

Report of the Activities of the House of Delegates—Dr. Charles E. Mongan, Middlesex South, senior delegate from Massachusetts.

This report (Appendix No. 3) was offered by Dr. Mongan. At the conclusion of the report Dr. Lee complimented Dr. Mongan on its completeness and ordered it to be made a part of the record.

Massachusetts Committee on Procurement and Assignment—Dr. Reginald Fitz, chairman, reporting through courtesy of the committee.

At the outset, in offering the report (Appendix No. 4) Dr. Fitz said that it was his understanding that his committee was a committee of the Massachusetts Medical Society.

Dr. Lee ruled otherwise pointing out that Procurement and Assignment Service is an agency of the government operating under the War Manpower Commission.

Dr. Fitz moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Public Relations—Dr. Albert A. Hornor, Suffolk, chairman.

This report, which was offered by Dr. Hornor, is as follows:

The committee met on August 18, 1943, at the Harvard Club and all were present except the representatives of two districts. President Lee presided, and I have the honor to report the following business as transacted:

1. The resignation of Dr. Elmer S. Bagnall, because he had become *ex officio* vice-chairman, and the election of myself as secretary of the committee.

2. The Committee on Public Relations endorsed in principle the plan of the Children's Bureau, as presented to the committee by Dr. Vlado A. Getting, for the care of wives and infants of men in the armed forces. This is the plan referred to in the advance information for the Council sent out by the secretary of the Massachusetts Medical Society. In the September 16, 1943 issue of the *New England Journal of Medicine* the plan is well described.

3. Dr. Bagnall asked that the members of the Committee on Public Relations submit to him the names of persons from their respective districts who would further the bank plan for postpayment of medical indebtedness, and this has been done.

4. A committee, consisting of Dr. Bagnall, Dr. Hornor and Dr. Tighe, was appointed by Dr. Lee to

confer with the Council on Employment Security The first meeting will be held October 7

Dr. Hornor moved the acceptance of this report The motion was seconded by a councilor

Dr. Schadt took issue with that part of the report as it refers to the last paragraph on page 3 of the sheets of advance information supplied the councilors, which reads as follows

The Committee on Public Relations met in conference with Dr. Vlado A. Getting, state commissioner of public health, who discussed the administration of this plan in Massachusetts. In this state all deliveries will be in a hospital. All deliveries will be by graduates of Grade A schools or by those approved by a technical committee, the latter committee for the most part is identical with the Committee on Maternal Welfare of the Massachusetts Medical Society

He pointed out that there are among the members of the Massachusetts Medical Society many who are graduates of unapproved schools. Under this plan, he continued, these gentlemen will not be permitted to take part in this plan.

Dr. Schadt was informed in this connection that the Massachusetts Department of Public Health had set up a technical committee, the personnel of which is largely made up from the Massachusetts Medical Society's Committee on Maternal Welfare and, when a graduate of a non-approved school applies to practice under this plan, his ability to do so will be assayed by this committee.

Dr. Schadt said that it was important that we understand that certain of our members could not practice under this plan unless they had received the approval of a committee.

Dr. Brainard F. Conley, Middlesex South, asked if it were not true that, when the law was passed in Washington, it was specified that there could be no discrimination as to the qualifications of men provided that they were within their rights to practice in the state in which they lived.

Dr. Lee said that the Attorney General of the United States had ruled that the Children's Bureau could not discriminate in the manner mentioned by Dr. Conley but this ruling was not binding on the states.

The Secretary pointed out that each state had its own administrative setup and that, when Dr. Getting met with the Committee on Public Relations, he said that he had a ruling from the Attorney General of Massachusetts to the effect that the Department of Public Health was within its rights, under the law, in setting up the conditions under which this plan should be operated in Massachusetts.

Dr. Mongan said he would not ask the Attorney General of Massachusetts, no matter how emi-

nent he might be, to decide a question of federal law.

Dr. Hornor said that there are two points at issue. In the first place, it is clear that federal boards cannot discriminate. On the other hand, in the actual administration of the plan in the several states, the health departments of those states are within their rights in designating those who will give their services under the plan. At least this is true in Massachusetts, Dr. Getting having the word of the Attorney General of Massachusetts to this effect.

Dr. Smith, a member of the Public Health Council, confirmed the latter statement in response to a question put by Dr. Schadt.

Dr. Donald Munro, Suffolk, was recognized by the chair. He said he would like to discuss certain other objections to this paragraph in the report of the committee.

As I understand it the recommendation of the committee is that this law be approved in principle. It seems to me that is wrong. I refer to the financial relation between the patient and his doctor. As I understand this law, there is a provision whereby the doctor is paid directly from the federal government or its representative, and there is no financial agreement between the patient and his doctor. A set fee is paid for certain services and that is given directly to the doctor without any intervention or consent on the part of the patient. Is that correct?

Dr. Hornor replied, 'The consent of the patient and the doctor must be agreed to; they must be in agreement before they make any application, and in making the application, they both sign a definite agreement as to that particular fee.'

Dr. Munro continued.

Nevertheless, the fee is paid directly to the physician by the Government and not by the patient. It seems to me that this violates a principle that we have supported for a great many years. I do not think that any member of the Massachusetts Medical Society will raise his hand to stop the law, but I do think it opens up that phase or aspect of the problem and I think for that reason that this law should not be approved in principle by this body. Furthermore, it seems that this is the opening wedge looking toward the establishment of state or federal medicine. Here we are now advocating in principle the payment by the federal government of money to the doctor without any formal agreement between the doctor and his patient. I think that is bad and it should be opposed by this society as a group. I am informed that practically every state society throughout the country has also taken that same attitude. They felt that this is a law which violates our principles. I recognize that regardless of any action of the Society the payment of these moneys and the putting into effect of this law will take place. But I think that this society should raise its objection to the violation of the principle involved. I hope that paragraph 2 of Dr. Hornor's report will not be accepted.

Dr. Hornor said that every member of the Committee on Public Relations felt the same way as Dr. Munro did. He said the committee was also aware that Dr. Munro's stand was the stand of the House of Delegates of the American Medical Association but that there did not seem to be any other way in which to put this proposal into effect.

Dr. H. Quimby Gallupe, Middlesex South, secretary of the State Board of Registration in Medicine, said he was instructed by his board to state that it would offer no objections to the plan proposed by Dr. Getting. He called attention, however, to the fact that there were a very large number of registered physicians in the Commonwealth who are graduates of unapproved schools and that there are many thousands of families being cared for by such graduates. He added that these families have within their numbers many citizens who contribute to the federal funds that support this plan. He thought that this matter would be better organized if the plan would indicate that all registered physicians in the Commonwealth could participate if they initially could prove to the Technical Committee their ability to do satisfactory obstetrics. An alternative to this, he continued, would be to have the plan open to all members of the Massachusetts Medical Society who could prove to the Technical Committee their ability to do satisfactory obstetrics.

Dr. Paul J. Jakmauh, Norfolk, was recognized by the chair. He said that the program under discussion was presented while he was commissioner of health of Massachusetts and that, as a result of a survey that he had made, he found that there was no need of it. He said that the plan would go on anyway whether we approved it or not and intimated that the Society should commit itself only after a free and thorough discussion of it.

Dr. Norman A. Welch, Norfolk, said that at the time the Massachusetts plan was first presented to the Committee on Public Relations, it had already gone to Washington for the approval of the Children's Bureau and that the reason for the haste in getting the Society's approval of it was a desire on the part of the Commissioner of Health to be able to say that the physicians of Massachusetts approved. He added that the plan, as outlined, did discriminate against certain physicians and in this respect we should move cautiously. We cannot, however, he continued, be in the position of failing to co-operate with the federal government in a plan that provides for the maternal and infant care of soldiers' dependents.

Dr. Smith explained that the haste mentioned by Dr. Welch was due to the fact that, under the law, the plan had to be in effect by September 1.

Dr. Conley expressed the thought that there are many principles involved in the plan and he wanted to know which of those we were accepting.

Dr. James C. McCann, Worcester, thought we might favor the program and leave the question of principles for another time.

Dr. Charles C. Lund, Suffolk, expressed himself as being in accord with many of the criticisms of the plan already mentioned. He thought, however, that it would be harmful to our public relations if the word went out that the doctors of the Commonwealth refused to play ball. He added that public relations might be further improved if we should ask the Children's Bureau and Dr. Getting to remove the apparent discrimination against certain doctors.

Dr. Richard Dutton, Middlesex East, asked whether the State Department of Public Health, in operating this plan, would act as a state body or as a federal body.

At the request of the chair, Dr. Smith answered by saying that the state department was merely distributing certain federal funds under regulations set up by this department. Dr. Hornor added that these regulations must be approved by the Children's Bureau, to which Dr. Smith agreed.

Dr. Leroy E. Parkins, Suffolk, said he was opposed to approving this thing officially. He added that he would like to co-operate but the way suggested did not appeal to him.

Dr. Elmer S. Bagnall, Essex North, president-elect, thought that this matter should for the moment be tabled until such time as action could be properly worded. He favored the appointment of a committee of the Council which would consider this matter, such a committee to report later in the meeting. Dr. Bagnall offered this as an amendment to Dr. Hornor's motion to accept the report. This amendment was seconded by a councillor.

There was much discussion at this point, principally as to procedure. Participating in the discussion were Dr. Lund, Dr. Philemon E. Truesdale (Bristol South), Dr. Schadt, Dr. McCann, Dr. Fitz, Dr. Nathaniel W. Faxon (Suffolk), Dr. Edward F. Timmins (Suffolk), Dr. Hornor and Dr. Mongan.

The chair called for a show of hands as to the advisability of receiving the report of the Committee on Public Relations without adopting what might be termed the recommendation contained therein. The vote was overwhelming in favor of such a procedure.

Dr. Lee declared the report received.

Dr. Hornor moved that the question of the care of the wives and children of men in uniform be

referred back to the Committee on Public Relations and that in the meantime the Society co-operate with the Commissioner of Public Health in the execution of the plan as now developed. This motion was seconded by a councilor.

Dr. Bagnall again reiterated his original thought that it would be much better if a committee of five of the Council were appointed by the President to bring in a report on this matter later in the meeting, such a committee to have in mind the discussion which has already taken place.

At the suggestion of the chair Dr. Bagnall acquiesced in offering this as a substitute motion. This substitute motion was seconded, and it was so ordered by vote of the Council.

The chair appointed Dr. Hornor, Dr. Smith, Dr. Bagnall, Dr. Welch and Dr. Gallupe. (These gentlemen retired.)

Committee on Legislation—Dr. Brainard F. Conley, Middlesex South, chairman.

No report.

Committee on New England Conference Anent Senate Bill 1161 (Wagner-Murray Bill)—

Dr. Walter G. Phippen, Essex South, chairman.

Dr. Phippen reported as follows:

The Executive Committee of the Council of the Massachusetts Medical Society empowered the President to appoint a committee to consult with representatives of the New England state medical societies regarding a joint conference between doctors and legislators of New England on the subject of the Wagner-Murray-Dingell Bill, with power to proceed with such a meeting if they so decided. The President appointed to that committee Dr. Walter G. Phippen, chairman, Dr. Frank R. Ober, Dr. Brainard F. Conley and Dr. Michael A. Tighe.

The committee met and decided to invite the New England state medical societies to send representatives to an informal meeting to discuss what steps if any should be taken, to influence the New England senators and representatives. In response to this invitation nine members of the medical societies of Maine, New Hampshire, Rhode Island and Connecticut met with your committee and the President of the Massachusetts Medical Society on Wednesday, September 22, 1943. While this conference was purely informal it was very satisfactory. Various angles of the situation were discussed and the viewpoints of the other states were well presented. It was the unanimous opinion of this group that it would be unwise, for various reasons, to try to hold a joint meeting of New England doctors and congressmen. It was, however, thought wise to consider the organization of an informal New England group to study and analyze the Wagner-Murray-Dingell Bill, and to distribute information and criticisms, possibly advice, as to the proper approach to senators and representatives, and send this to various members of the profession throughout New England with the idea that personal contact might do more good than large

conferences. With this end in view the meeting adjourned to meet again on October 20.

On a motion by Dr. Phippen and a second by a councilor the report was accepted as a report of progress.

Committee on War Participation—Dr. William B. Breed, Suffolk, chairman.

This report (Appendix No. 5) spoke in terms of appreciation of the work done by the district reviewing committees. It said that 321 names were submitted to these committees and 298 had been reported on; 102 were declared available, 31 were already in the service and 32 had already submitted their applications. Twenty-nine were declared essential, and 104 were not available.

The report recommended that the present reviewing committees in the several districts be not discharged, but be retained with the same personnel and organization (chairmen and secretaries) as district committees on war participation, subcommittees, so to speak, of this committee.

Dr. Breed moved the adoption of the recommendation. This motion was seconded by Dr. Mongan, and it was so ordered by vote of the Council.

The report further recommended that an appropriation of \$300 be made to this committee for past and future expenses, largely clerical, from the time of its appointment to January 1, 1944.

Dr. Breed moved the adoption of this recommendation. The motion was seconded by a councilor.

The Secretary announced that the Committee on Finance approved, and it was so ordered by vote of the Council.

Committee on Postwar Loan Fund—Dr. George Leonard Schadt, Hampden, chairman.

This report (Appendix No. 6) was offered by the chairman who moved its acceptance as a report of progress. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Committee on Public Relations (continued)

Dr. Hornor, in reporting for the committee of five appointed earlier in the meeting, made the following motion:

The Council of the Massachusetts Medical Society pledges full co-operation with the Massachusetts Department of Public Health in the procurement of adequate care for the wives and infants of men in the armed forces. The Council respectfully requests that the Commissioner of Public Health modify the regulations with reference to "Standards of Medical Care," paragraph 2, as printed in the *New England Journal of*

Medicine for September 16, 1943, so that the physician who is to be paid for maternal or infant care must be registered in Massachusetts and must be found qualified by training or experience in obstetrics or pediatrics and approved by the technical committees appointed by the Commissioner of Public Health.

Dr. Hornor moved the adoption of this motion. The motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee to Meet With the Medical Advisory Committee of the Industrial Accident Board — Dr. Daniel J. Ellison, Middlesex North, chairman.

No report.

Subcommittee on Tax-Supported Medical Care — Dr. Elmer S. Bagnall, Essex North, chairman.

This report, which was offered by the chairman, is as follows:

The State Department of Public Welfare has, with the approval of its advisory board, adopted a formulary of approved drugs. This is based on pharmacopoeal rather than more expensive proprietary remedies.

The druggists are co-operating effectively.

We recommend that the Council of the Massachusetts Medical Society approve the formulary in principle and that physicians treating old-age and state-welfare patients be urged to accept the initial minor inconveniences as a public service in the interest of proper economies.

Dr. Bagnall moved the adoption of the recommendation. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Subcommittee on Postpayment Medical Care (Bank Plan) — Dr. Elmer S. Bagnall, Essex North, chairman.

Dr. Bagnall said that the committee was to have a meeting at the close of the Council meeting and that a vice-president of the National Shawmut Bank is endeavoring to obtain material for the committee from the National Bank Association. Dr. Bagnall moved that this report be adopted as a report of progress. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Subcommittee on Prepayment Medical-Care Costs Insurance — Dr. James C. McCann, Worcester, chairman.

Dr. McCann reported as follows:

When I reported in June there were about 2000 members enrolled. The early period of organization was necessarily given over to approaching industrial groups, and I can say that our enrollment now in the first year will be 10,000. That compares very favorably with all the states except one. New Jersey in the

first year had about 7000, and Colorado in about the same period had 10,000 and is concerned with whether it can go much beyond that. Pennsylvania in three years has approximately 10,000 enrollments. Michigan must be looked on as most unusual because of its huge organized industries. Its enrollment is running up to 500,000.

With regard to the financial condition of the organization, last June the subscriptions were \$6000. Today they stand at \$30,000. The operating expenses are about \$11,000 and the payments to members to date about \$10,000, which, other than that initial cost of \$4000 for organization expense, leaves the Massachusetts Medical Service Corporation with a balance of \$1200. That takes care of the \$300 required for the premium and the 25 per cent reserve required by the Commissioner of Insurance. It may possibly be that the reserve will be waived for the first year, which would allow us to remove the obligation of the \$4000, probably about \$4000 surplus, without having to use any of the \$25,000 that the Council so generously donated. So that we have our program rolling along at about the average rate, and rolling along with every prospect of success.

Dr. McCann's complete report (Appendix No. 7) was read by title only.

Dr. McCann moved that the report be accepted as a report of progress. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Military Postgraduate Committee — Dr. W. Richard Ohler, Norfolk, chairman.

No report.

Committee to Aid the District Rationing Administrator — Dr. Joseph Garland, Suffolk, chairman.

Dr. Garland reported as follows:

Your committee, since notification of its appointment on June 21, has met four times with the district rationing officer; Mr. John M. Deely, and Miss Elizabeth Golden, of the Food Rationing Division. About 730 persons, up to October 1, have applied for unusual allotments of rationed foods on Doctors' Certificates of Patients' Necessity, of which 240 have been reviewed in detail by the members of the committee. The remainder were passed on at the district office under instructions laid down by the committee. Between 20 and 30 certificates were rejected. In addition to these requests, several thousand certificates have been approved by the local war price and rationing boards according to directions furnished by the committee.

At the present time, certificates are coming in at the rate of approximately 150 per month, which perhaps is not an unusual number to come from an area with over 3,000,000 inhabitants, and would seem to indicate that the medical profession as a whole is co-operating well with the rationing officials. There will probably be a sharp increase from now on, however, as the district has been enlarged, as of October 1, to cover the entire state, adding some 2,000,000 individuals to the program.

It seemed desirable at the start to establish certain reasonable maximums of rationed foods that would apply to the majority of cases, regardless of the medical diagnosis, and your committee, after consulting with various competent authorities, accepted the standards established by Joslin and others for diabetics, namely, 32 pounds of processed foods and 40 of meats and fats for each two-month period. Local rationing boards have been advised that they may grant up to these maximums on certificates properly executed by registered physicians. All requests in excess of these maximums are forwarded to the district office for review.

It is obviously not the function of this committee to decide in what manner and by what method medicine is to be practiced in Massachusetts, but only to prevent abuse of the privilege of prescribing extra rations, so that a limited supply of certain foods may be fairly distributed.

So far as local district rationing officials have been able to discover, Massachusetts is the only state that has made the effort to handle the requests for extra food rations in this manner.

Dr Garland moved the adoption of the report. This motion was seconded by a councilor and it was so ordered by vote of the Council.

Committee to Aid the Boston Medical Library—
Dr William H Robey, Suffolk, chairman

Dr Robey reported that the work of the committee had been finished. He moved that it be discharged. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Cancer—Dr Ernest L Hunt, Worcester, chairman

No report

Committee on Postgraduate Instruction—Dr Reginald Fitz, Suffolk, chairman

No report

Committee on Physical Therapy—Dr Arthur L Watkins, Middlesex South, chairman

No response

Committee on Expert Testimony—Dr Frank R Ober, Suffolk, chairman

No report

Committee on Automobile Insurance Claims—
Dr Henry C Marble, Suffolk, chairman

No response

Committee on Convalescent Care—Dr T Duckett Jones, Norfolk, chairman

No response

Committee to Study the Practice of Medicine by Unregistered Persons—Dr Richard Dut

ton, Middlesex East, chairman

No report.

Committee to Meet With the Massachusetts Hospital Association—Dr. Walter G. Phupen, Essex South, chairman.

No report.

Committee on Maternal Welfare—Dr Judson A Smith, Suffolk, chairman

No response

Committee on Rehabilitation—Dr William E Browne, Suffolk, chairman

The report which was offered by Dr Browne is as follows

This communication is obviously not a report from the Committee on Rehabilitation. Even though quite frequently in the daily press and various professional, including medical, journals the need for rehabilitation is being stressed more and more, no meeting of your committee has been held since the last meeting of the Council of the Massachusetts Medical Society.

Curtis M Hillard, director of the Subdivision of Health, Massachusetts Committee of Public Safety, called a meeting of his fairly large committee on September 14, 1943. Only four members of his committee, however, answered his call. He has again notified all members of his committee that an important meeting will be held October 8. Shortly after this meeting the members of your committee will get together and try to arrange a program that may be of some help in this important work of rehabilitation.

It may be of interest herein to state that already it seems apparent that the members of the Massachusetts Medical Society can be of real assistance with the formation of a group of physicians in each district who may review, when called on to do so, the medical problem of anyone discharged from service because of some form of disability. At the present time it does not seem that the members of the Massachusetts Medical Society can do very much in the matter of aiding those discharged, even when rehabilitated in getting a job. With information at hand it is not entirely clear what the federal government will do in this matter. Certain states have gone ahead with tentative programs, but no very definite program has been worked out thus far.

I repeat that following the meeting on October 5 the Committee on Rehabilitation will meet and, if necessary, send a communication to the Executive Committee of the Council of the Massachusetts Medical Society before the next general meeting of the Council.

On a motion by Dr Browne and a second by a councilor the report was accepted as a report of progress.

Committee on Ways and Means to Conserve Physicians' Energies—Dr Elmer S Bagnall, Essex North, chairman

No report

APPOINTMENTS

Dr Lee named Dr Fritz B Talbot, Suffolk, chairman of the Auditing Committee for 1943 and

Dr. Harry Linenthal, Norfolk, as the second member of this committee. These nominations were confirmed by vote of the Council.

The following ad-interim appointments, made by the President, were confirmed by vote of the Council:

To the Council:

- Dr. John T. Batal, Essex North, replacing Dr. Elmer S. Bagnall, who has become a member *ex officio*.
- Dr. John E. Burns, Norfolk, replacing Dr. Norman A. Welch, who has become a member *ex officio*.
- Dr. Joseph H. Carey, Norfolk, replacing Dr. Louis F. Curran, deceased.
- Dr. Henry M. Landesman, Norfolk, replacing Dr. Morris Frank, deceased.
- Dr. Nahum R. Pillsbury, Norfolk South, replacing Dr. Daniel B. Reardon, who has become a member *ex officio*.

To the Committee on Finance:

- Dr. Francis C. Hall, chairman, replacing Dr. John Homans, resigned.

To the Committee on Legislation:

- Dr. William E. Browne, Suffolk, replacing Dr. William B. Breed, resigned.
- Dr. John J. McNamara—representative from Plymouth District.
- Dr. Henry Wardle—representative from Bristol South District.

To the Military Postgraduate Committee:

- Dr. Gordon M. Morrison.

To the Committee on Postpayment Medical Care (Bank Plan):

- Barnstable: Dr. Harold F. Rowley
- Berkshire: Dr. Charles F. Fasce
- Bristol North: Dr. James H. Brewster
- Bristol South: Dr. Harold E. Perry
- Essex North: Dr. Elmer S. Bagnall, chairman (already a member of committee)
- Essex South: Dr. Loring Grimes
- Franklin: Dr. Howard M. Kemp
- Hampden: Dr. Patrick E. Gear
- Hampshire: Dr. Alfred J. Bonneville
- Middlesex East: Dr. Wilfred L. McKenzie
- Middlesex North: Dr. Daniel J. Ellison (already a member)
- Middlesex South: Dr. Egon E. Kattwinkel
- Norfolk: Dr. Norman A. Welch
- Norfolk South: Dr. Walter L. Sargent
- Plymouth: Dr. Michael F. Barrett
- Suffolk: Dr. Francis T. Jantzen
- Worcester: Dr. James T. Brosnan
- Worcester North: Dr. William G. LeBrecht

To the Postwar Loan Fund Committee:

- Drs. George L. Schadt, chairman, Edward P. Bagg, C. Sidney Burwell, John Homans, Eliot Hubbard, Jr., Peirce H. Leavitt, Herbert L. Lombard, Hyman Morrison, Walter G. Phippen, William F. Ryan, David D. Scannell, Charles A. Sparrow, Ralph R. Stratton, Michael A. Tighe, Charles F. Wilinsky.

To the Committee Concerned with Prepayment Medical Care Costs Insurance:

- Dr. Joseph C. Merriam, replacing Dr. William B. Breed, resigned.

To the Committee on Public Education:

- Dr. Joseph Garland, replacing Dr. Richard M. Smith, resigned.

To the Committee on Public Relations:

- Dr. Harold R. Kurth, replacing Dr. Elmer S. Bagnall, who has become a member *ex officio*.

To the Committee to Aid the District Rationing Administrator:

- Dr. Joseph Garland, chairman, Dr. F. Gorham Brigham, Dr. Franklin W. White.

To the Committee to Arrange Conference with New England Physicians Anent the Wagner-Murray-Dingell Bill:

- Dr. Walter G. Phippen, chairman, Dr. Frank R. Ober, Dr. Brainard F. Conley, Dr. Michael A. Tighe.

To Massachusetts Hospital Service, Incorporated (voting member):

- Dr. Joseph C. Merriam, replacing Dr. David L. Halbersleben, resigned.

NEW BUSINESS

The chair recognized Dr. Harold L. Musgrave, Suffolk. The latter asked that the letters from Dr. Ru. hmore and Mr. Wragg, referred to in the report of the Executive Committee, be read.

These letters were read by the Secretary. They are as follows:

MIDDLESEX UNIVERSITY SCHOOL OF MEDICINE
May 25, 1943.

Dr. Michael A. Tighe, Secretary
Massachusetts Medical Society
8 The Fenway
Boston, Massachusetts
Dear Dr. Tighe:

The Massachusetts Medical Society has from time to time formally directed its attention to the School of Medicine of Middlesex University, and it is the opinion of the school that the time has come for the Society to do so again. The grounds for this opinion are set forth below, after reviewing some of the past occasions.

In 1936, a law was passed in Massachusetts establishing an approving authority for medical schools, and in accordance with this statute, no graduate of a medical school not approved by this authority should after a certain time, be admitted to examination for license to practice medicine in this Commonwealth. The effect of this law on Middlesex Medical School was to stimulate the efforts at improvement which had previously seemed to be rather desultory and separated by rather long intervals of time. In that same year a letter was written to the Massachusetts Medical Society by Middlesex College in which it was indicated that the good offices of the Society in plans for improving the school would be appreciated.

The Committee on Medical Education and Medical Diplomas, of which Dr. Reginald Fitz was chairman, presented as part of its report to the Council at its stated meeting held October 7, 1936, the following recommendations: "That the Massachusetts Medical Society inform the Trustees of Middlesex College that the Society is deeply interested in the improvement of all conditions which have to do with the giving of medical education in Massachusetts; that the Society is anxious to do all that it can to help Middlesex College develop in an approved manner. The Society suggests that the Trustees of Middlesex College lay before the president of the Society suggestions as to how the Massachusetts Medical Society might be of help to Middlesex College."

The proceedings of the Council read further as follows: "In addition to the foregoing formal recommendation the committee offered the suggestion that the President be empowered to appoint a committee of fellows of the Massachusetts Medical Society to act on behalf of the Society in an advisory capacity to any medical school or college in helping direct such institution's efforts to develop and improve its facilities for teaching. The report of the committee was accepted by vote. The Council next adopted the formal recommendation of the committee and voted approval of the suggestion that the President appoint an advisory committee recommended by the Committee on Medical Education and Medical Diplomas."

In June, 1939 Dr Elliott Joslin, recognizing that the Society had an important interest in all efforts directed toward the education of physicians within the Commonwealth, and therefore had some obligation in the matter and being aware of a certain expressed willingness on the part of the school to accelerate its progress devoted a considerable part of his annual discourse before the Society to the discussion of the problem presented by Middlesex School of Medicine and he made a number of suggestions noting some steps to be taken by the college.

Actually so little seemed to be done following the action of the Council in 1935 and following the suggestions made by Dr Joslin in 1939 that the general impression has been that nothing was accomplished. But it was important that the problems should have been brought to the attention of the medical profession and be discussed frankly and freely. It became more evident that there was a problem in which the medical profession had a great interest and since the law said in substance that the school would within a comparatively short time have to be salvaged or closed more serious attention was given to the question of whether the school should be salvaged and if not why not.

Without going into the details of a rather complicated situation it may be summarized by saying that the impression spread that the school was willing to be salvaged by the efforts of others rather than by its own efforts and many persons raised the question "Why bother about the school if it was not willing to help itself?"

It is because this impression was not quite correct that the school would like to bring to the attention of the Society the condition in which it actually now is so that the Society may become aware of how much has been accomplished by the school in transforming itself and in making progress on the way to deserving approval.

The basic criticism of the school was its proprietary character. Assurance can be given that in this respect the change has been radical and complete. The proprietary features have been removed and will not be permitted to return.

Another criticism was that the standards of admission were low. For a number of years until the present war emergency, the requirements were a baccalaureate degree and the generally accepted minimum requirements in science as set by the Council on Education of the American Medical Association. The quality of the students at judged by scholastic standards in college has been steadily improving.

Another criticism was that Middlesex accepted students who had failed elsewhere. For a number of years no student who failed in another medical school has been admitted to advanced standing. Occasionally a student from this group has been admitted to the first year class but no credit is given for any work done in another medical school if the candidate has been dropped on account of poor scholarship.

Another criticism has been that graduates of schools of osteopathy were admitted to advanced standing and were given their degrees in medicine after one year of attendance. This practice was especially objectionable because to few osteopathic physicians had fulfilled the usual minimum premedical requirements. For a number of years no credit toward the medical degree has been given by Middlesex for work done in a school of osteopathy.

The status of the graduates has been improved as they are now eligible for commissions in the armed forces and over two hundred have actually been commissioned. The students and the faculty have been given deferment of over \$18,000 of the War Loan Fund has been given to Middlesex students.

Certain much needed improvements it has been impossible to complete under wartime conditions but plans are in the making for rapid development as soon as conditions permit. The demand for medical education has not diminished and the school is still overcrowded but the instruction in the first and second years is good. It is in the third and fourth years that serious deficiencies persist due to a lack of clinical facilities.

There has been expressed a fear that hospitals approved by the Council on Medical Education of the American Medical Association would lose their standing with this body if they permitted the use of their clinical facilities for the teaching of the students of Middlesex. The secretary of the council, Dr Herman G. Weinkotten has stated explicitly that so far as the rating by the council is concerned such teaching of students would have no effect. Thus this difficulty has not been removed.

One of the great obstacles to the progress of the school has been the adverse sentiment of the medical profession largely due to the just criticism based on the points which have been noted above but the grounds for which are now things of the past.

The school is prepared and will be very glad to enter into conference with the Massachusetts Medical Society along the lines suggested by the Committee on Medical Education and Medical Diplomacy in 1936 or in any other way that seems appropriate to the officers of the Society and we hope that the Society is as well now as it was in 1936 to assist the school in such ways as may seem practicable.

Yours sincerely,

Stephen Rushmore (signed)

STEPHEN RUSHMORE, M.D. Dean

MIDDLESEX UNIVERSITY

August 16, 1943

Dr Michael A. Tighe, Secretary
Massachusetts Medical Society
3 The Fenway
Boston, Massachusetts

Dear Dr Tighe

Several times in the past the Massachusetts Medical Society has expressed its willingness to be of assistance to Middlesex University School of Medicine. We believe

now that the time has come when your society may aid us in a very material way.

The Executive Committee of the Board of Trustees, as at present constituted, has during the past year made considerable improvement in the medical school, and is now much in need of the assistance which the Executive Committee believes the Massachusetts Medical Society may give. This point of view, I believe, has been presented to your society by our dean, Dr Stephen Rushmore, on May 25, 1943, and since time is important we should now greatly appreciate your appointing a small committee to meet with a similar committee of the university at an early date.

The School of Medicine is training several hundred students for eventual service as commissioned officers in the United States Army Medical Corps. It is greatly handicapped in its efforts by the lack of adequate clinical teaching facilities. The trustees of the university ask the Massachusetts Medical Society for assistance in order that the university may provide a better training for these prospective physicians, whose services are so vitally needed, as indicated by the leading editorial, entitled "More Doctors Needed for the Armed Forces," in the August 7 issue of the *Journal of the American Medical Association*.

Very truly yours,

Samuel H. Wragg (signed)

SAMUEL H. WRAGG, President

The Secretary said for the information of the Council that on October 7, 1936, the following motion was passed by the Council:

That the Massachusetts Medical Society inform the Trustees of Middlesex College that the Society is deeply interested in the improvement of all conditions which have to do with the giving of medical education in Massachusetts, that the Society is anxious to do all that it can to help Middlesex College develop in an approved manner. The Society suggests that the Trustees of Middlesex College lay before the president of the Society suggestions as to how the Massachusetts Medical Society may be of help to Middlesex College.

He continued that, under this motion, the following committee was appointed. Dr. Reginald Fitz, chairman, Boston; Dr. Fresenius Van Nuys, Weston; Dr. James F. Donaldson, Salem; Dr. William F. Lynch, Worcester; Dr. William T. Frawley, Pittsfield. He added that there is no record that this committee has ever reported.

Dr. Musgrave spoke of the radical changes which had taken place in the personnel of the trustees of Middlesex University Medical School. He said that the old order is gone forever, that this school has ceased to be a proprietary school and that it is now in the hands of honest and earnest men who want to do and who are doing a good job. He added that facilities for clinical teaching represents the school's greatest need. He pointed out that the graduates of this school are being commissioned in the Medical Corps of the United States Army.

Dr. Musgrave moved that the committee, here before referred to as appointed in 1936, be dis-

solved. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Dr. Musgrave moved that a committee be appointed to discuss with the trustees of Middlesex University their problems in their attempted improvement of the school. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Dr. Earle M. Chapman, Suffolk, was recognized by the chair. He spoke as follows:

At the May meeting of the Council many of you applauded the report of the Committee on Legislation in which we were advised that only \$50 was spent on legal aid. It is unfortunate that you who applauded did not also hear Dr. Quimby Gallupe, secretary of the Board of Registration in Medicine, expose the shocking inadequacies of our legislative committee in the May 27 meeting. In this year's session, a relatively inactive year, two bills of great importance to the Massachusetts Medical Society went through without either the support or opposition of our society.

First, the Antivivisection Bill reached the Governor's desk, where it fortunately was stopped by him. This bill was not opposed.

Second, a vital bill to improve the standards of practice in this state was defeated. This was a bill which would limit to the number of three the times that a man could appear before the Board for re-examination. This bill received no support from the Committee on Legislation and, as Dr. Gallupe expressed it, he likes to feel that the Board of Registration functions in the State House for the Massachusetts Medical Society. In closing his address at that time Dr. Gallupe made two specific recommendations to the Society: that we employ adequate legislative counsel, and that, in order to improve the standards of practice, we favor the annual registration of physicians.

Dr. Chapman moved that the Council of the Massachusetts Medical Society recommend employment of adequate legislative counsel to aid legislation favorable to the medical profession and to oppose legislation that is considered unwise. This motion was seconded by a councilor.

Dr. Welch asked if this motion were passed would it compel the Committee on Legislation to employ counsel irrespective of its judgment as to the necessity for such employment. Dr. Lee replied that such was his understanding of the motion.

Dr. Lester M. Felton, Worcester, asked what was the meaning of the words "adequate counsel" as they appear in the motion. Dr. Chapman replied that these terms refer to a lawyer who makes the serving of our interests a full-time job or mostly a full-time job, who will make it his business to be up at the State House and work in our interests as a lawyer.

Dr. Cyril M. Lydon, Norfolk, asked if the problem had not in the past been cared for by the committee which handles our legislative matters.

Dr. Lee asked Dr. Brainard F. Conley, chairman of the Committee on Legislation, to come forward and be heard. He further asked that Dr. Conley say something about the historical development of the present committee. Dr. Conley spoke as follows:

I thought that the day had come when all reverberations of dissension and personal feelings had gone. I thought the day had come when the Massachusetts Medical Society was being represented by men who had at heart only the interests of the public in general and that of their fellow practitioners. I thought that this laudable object was accomplished this past year. It was accomplished by and as the result of a new setup—a committee which is now no longer a junior committee but a committee which is appointed as truly representative, a democratic group of men—one man from each district who is elected by each district, and they together elect a chairman and a clerk. That committee met and elected as chairman myself, and elected as secretary Dr. Lester M. Felton, of Worcester—and a no more conscientious man is in this society than Dr. Felton.

We have the full co-operation of every member of your committee. We had unanimous action on every bill that was discussed. It is one of the most pleasant assignments that I have ever had on any committee. And as a result of our work we returned to this Society a goodly portion of the amount of money which we asked for at the beginning.

The reason for that return of money was that we did not need to spend it. We were not spending it for any purpose other than actual need. We were not giving away the money of the Society. We were not seeking any outside assistance unless that assistance was needed; and when that assistance was needed, we consulted an attorney in a firm in Boston. Now, it is in the by-laws that in order to have counsel or engage the services of legal counsel it is necessary for the Committee on Legislation to get permission from the President. That was done. I know it was done because I did it myself by calling Dr. Schadt, your president, at his home in Springfield and told him the point had come when we needed the services or the opinion of legal counsel, and Dr. Schadt immediately gave me permission to engage counsel, which we as a committee felt we needed. And he gave me permission to engage counsel who had been agreed upon by the five working members of the committee, namely, Dr. William Breed, Dr. John Fisher, Dr. Lester Felton, Dr. Charles McCann and myself. That was the working committee.

Now, then, \$1500 was the price which was proposed. We did not feel that it was necessary to spend \$1500 for legal assistance, and I discussed with our committee of five the possibility of needing an attorney or legal counsel. We decided to ask legal counsel from the firm of Powers and Hall, attorneys in Boston—attorneys who handle, perhaps, 70 per cent of all malpractice cases. Mr. Leland Powers has appeared before many district societies as a speaker on medical aspects of laws and legislation; and I believe there is no more competent legal concern in Boston to give aid to us. That firm of attorneys was asked for counsel, with the limitation that we would pay

them for what advice we got or needed and not on any established yearly basis or fee

I spent one afternoon in the office of Powers and Hall and went over every bill which seemed to require legal counsel or legal advice. I spent from 2 30 until 6 15 in that office with Mr James M Clark, a graduate of Harvard University in the Class of 1904 and Harvard Law School later, and a man who graduated with honors and is regarded by the legal profession of the United States as an authority. That cost us \$50. It necessary, your committee would have spent the entire amount the Council had given us if we needed it—but we did not need it.

Now, then, regarding the matter of the three bills of the Board of Registration in Medicine, I have been beside the secretary of the State Board of Registration in Medicine at this meeting. At the request of Dr Qumby Gallupe, the secretary of the State Board of Registration in Medicine, I personally appeared at the State House at the hearing given by the Committee on Public Health on those bills, and I personally—and Dr Gallupe is present and will bear me out—put the Massachusetts Medical Society on record as favoring those three bills.

Now, on the antivivisection bill, that bill was heard before the Committee on Public Health. I was present at that hearing and I listened to the arguments pro and con, and I put the Massachusetts Medical Society on record as opposing that antivivisection bill.

Your Committee on Legislation has had a recording on every bill that came before the Committee on Public Health. That is a matter of record with the clerk Norman F Wellen, of Marlboro. On every bill that pertained to medicine there was an appearance or a recording of the Massachusetts Medical Society.

I have no apologies to make for my committee or for myself for any bit of our conduct in representing you during the past legislative year.

Dr Chapman's motion was put by the chair and defeated by vote of the Council.

Dr Chapman moved that the Council of the Massachusetts Medical Society favor the annual registration of physicians in order to further maintain the standards of practice. This motion was seconded by a councilor.

Dr Welch asked to be recorded as opposed to this motion.

Dr Chapman expressed a desire to hear Dr Gallupe on the motion. At the invitation of the chair, Dr Gallupe came forward and spoke as follows:

For the second time I am here but I did not come until asked to do so. The Board of Registration in Medicine has felt that it would be of some help to have in annual registration or reregistration of physicians because it was found that it has been of some help for nurses and dentists. It has seemed to us that there was not in our office at the State House sufficient information about physicians who have registered to practice in the Commonwealth. We register a physician once and he is forever registered unless he does something wrong and after we register him we have no further information about him of any nature. We do not know whether he has continued to practice

medicine or not. We have no information about him. We do not know anything more except that he has registered to practice and none of the doctors in his city or town know much more about him.

Now recently because of the war, we have corresponded with the Red Cross the FBI and the Army and Navy about physicians and we cannot give them any information. All we can give them is the name and nothing more for the past twenty or thirty years. And so we thought that an annual registration on the doctor's birthday would be of some help. It might be of help in tracking down some physician who is practicing illegally. We do not know how many there are and you do not know because you have no means of ascertaining. If you had a list on your desk of registered physicians, you could readily tell who was not registered. It might be some help in tracking down these men who practice illegally in the Commonwealth. That is of some value, I think. We think it would be of value to the Society as it would enable it to know who is registered to practice. It is just a suggestion but, as Dr Rushmore said last spring, we do not want to do anything that the Society does not want to have us do or does not like to have us do. We want to do whatever is most helpful. We are your agents. We, as members of your Society, wish to do what you would like to have us do. If you do not want the annual registration, we do not want it. If you do want it, we will help to get it for you. That is all.

Dr Carl Berse, Norfolk thought this was an inappropriate time to bring up a matter of this kind. He moved that the motion be tabled. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

At 2 15 p.m., Dr Parkins moved that the meeting be adjourned. This motion was seconded by a councilor and it was so ordered by vote of the Council.

MICHAEL A. TIGHE, Secretary

APPENDIX NO 1

ATTENDANCE

BARNSTABLE	I D Cudner
W D Kinney	H F Perry
	I F Shry
BERKSHIRE	P F Truesdale
	H W Wardle
	LEXINGTON
I S F Dodd	J S Bignall
C F Kernan	R V Bicketel
C T Leche	I F Bital
J I McLaughlin	N F D Cesare
P J Sullivan	F H Ganley
BRISTOL NORTH	R C Hannigan
W H Allen	H R Kurth
J H Brewster	P J Look
R M Chambers	R J Neil
W J Morse, Jr	R C Norris
W M Stollis	I Richardson
BRISTOL SOUTH	C W Snow
G W Blood	C I Warren
R B Butler	

ESSEX SOUTH

Bernard Appel
Loring Grimes
P. P. Johnson
A. E. Parkhurst
W. G. Phippen
E. D. Reynolds
H. D. Stebbins
P. E. Tivnan
J. W. Trask
C. F. Twomey

FRANKLIN

F. J. Barnard
A. W. Hayes
W. J. Pelletier

HAMPDEN

E. H. Allen
E. P. Bagg
W. C. Barnes
H. F. Byrnes
J. L. Chereskin
G. B. Corcoran
E. C. Dubois
Adolph Franz, Jr.
G. L. Gabler
P. E. Gear
G. D. Henderson
F. S. Hopkins
E. A. Knowlton
M. W. Pearson
A. G. Rice
G. L. Schadt

HAMPSHIRE

A. N. Ball
A. J. Bonneville
W. M. Dobson

MIDDLESEX EAST

J. H. Blaisdell
C. W. De Wolf
Richard Dutton
E. M. Halligan
R. W. Layton
M. J. Quinn
R. R. Stratton

MIDDLESEX NORTH

W. M. Collins
D. J. Ellison
A. R. Gardner
W. F. Ryan
M. A. Tighe

MIDDLESEX SOUTH

C. F. Atwood
E. W. Barron
W. B. Bartlett
Harris Bass
J. M. Baty
J. D. Bennett
E. H. Bigelow
G. F. H. Bowers
Madelaine R. Brown
R. W. Buck

E. J. Butler
J. F. Casey
B. F. Conley
H. F. Day
C. L. Derick
C. W. Finnerty
H. Q. Gallupe
Stanton Garfield
H. G. Giddings
J. L. Golden
A. D. Guthrie
Eliot Hubbard, Jr.
F. R. Jouett
A. A. Levi
A. N. Makechnie
Dudley Merrill
C. E. Mongan
J. P. Nelligan
Dwight O'Hara
Fabyan Packard
L. G. Paul
S. H. Remick
E. H. Robbins
M. J. Schlesinger
E. W. Small
A. B. Toppan
J. E. Vance
C. F. Walcott
Hovhannes Zovickian

NORFOLK

Carl Bearse
Arthur Berk
M. I. Berman
J. E. Burns
J. H. Carey
D. J. Collins
F. P. Denny
G. L. Doherty
Albert Ehrenfried
Susannah Friedman
J. B. Hall
H. B. Harris
R. J. Heffernan
P. J. Jakmauh
I. R. Jankelson
C. J. Kickham
E. L. Kickham
H. M. Landesman
C. M. Lydon
H. L. McCarthy
R. T. Monroe
F. J. Moran
Hyman Morrison
M. W. O'Connell
G. W. Papen
S. A. Robins
D. D. Scannell
J. A. Seth
Kathleyne S. Snow
J. W. Spellman
J. P. Treanor, Jr.
W. J. Walton
S. H. Weiner
N. A. Welch

NORFOLK SOUTH

D. B. Reardon

PLYMOUTH

G. A. Buckley
P. H. Leavitt
J. J. McNamara
G. A. Moore
E. L. Perry
W. H. Pulsifer

SUFFOLK

W. B. Breed
W. E. Browne
G. C. Caner
E. M. Chapman
David Cheever
Pasquale Costanza
N. W. Faxon
G. B. Fenwick
Jacob Fine
Reginald Fitz
Channing Frothingham
Joseph Garland
A. A. Hornor
H. A. Kelly
R. I. Lee
C. C. Lund
Donald Munro
H. L. Musgrave
H. F. Newton
F. R. Ober
F. W. O'Brien
J. P. O'Hare
L. E. Parkins
L. E. Phaneuf
Helen S. Pittman
W. H. Robey
H. F. Root

R. M. Smith
M. C. Sosman
E. F. Timmins
J. J. Todd
S. N. Vose
Conrad Wesselhoeft
C. F. Wilinsky

WORCESTER

C. R. Abbott
B. H. Alton
B. F. Andrews
A. W. Atwood
George Ballantyne
W. P. Bowers
P. H. Cook
G. A. Dix
J. J. Dumphy
John Fallon
L. M. Felton
E. R. Leib
L. P. Leland
W. F. Lynch
J. C. McCann
A. E. O'Connell
H. L. Paine
R. S. Perkins
O. H. Stansfield
R. J. Ward
R. P. Watkins

WORCESTER NORTH

E. A. Adams
H. D. Bone
C. B. Gay
G. P. Keaveny
F. A. Reynolds

APPENDIX NO. 2

REPORT OF THE COMMITTEE ON ETHICS AND DISCIPLINE

During the past four months, the committee has held two all-day meetings on June 30 and on September 15, with a special meeting on August 16. During this time, numerous cases have come to the attention of the committee. Some of these were of very minor importance and were settled by letter. Several others required considerable investigating, hearings being given to both complainant and defendant. These complaints were settled amicably by the committee.

A number of communications from laymen complaining of the amounts of doctors' charges, mostly for small amounts, have been received and have been answered invariably that it was not within the province of this committee to decide matters of professional fees, which should be settled satisfactorily between doctor and patient.

Three charges by laymen against doctors for alleged breach of ethics, after exhaustive investigation, were decided unanimously for the defendants.

There were three other cases of such a serious nature that a brief résumé at this time is justified.

Case 1. A charge of breach of ethics in an attempt to discredit and injure the professional reputation of some of his confreres was brought against a fellow. Accompanying this complaint were several items on which the complaint was based. Thorough investigation was given

o this charge and every possible avenue of approach was explored, but no actual proof which would stand the scrutiny of a board of trial or of a court of law could be verified, and the committee was forced, therefore, to place the case on file. The complainants were notified.

Case 2 There was a complaint by two fellows against a third charging active attempts to belittle their reputations and their professional standing in the community by active participation in the preparation of and unfair and vicious testimony during a court case for malpractice. Following a period of investigation covering two months, including scrutiny of court records, hospital records and hearings given to both the complainants and the defendant, an overwhelming mass of proof was accumulated resulting in a unanimous vote by the committee of guilty, and the fellow was requested to resign from the Society. His resignation was received and accepted.

Case 3 This case is the first of its kind that has been brought to the attention of the committee during the past eight years. A complaint was received from a layman in good standing and of excellent reputation in the community in which he lives, against a fellow practicing in the same community, charging violation of Chapter III, Article I, Sections 1 and 3, of the *Principles of Medical Ethics* of the American Medical Association. It is not the duty of the Committee on Ethics and Discipline to intrude itself on the private life of any member. That is a matter between himself and his conscience and his self respect. But when that private life becomes a public reproach on the Society sufficiently grave to be complained about by laymen, then it is our duty to investigate. Inquiries and conversations with the defendant and corroboratory evidence given unwillingly by his confreres, in writing, and the fact that on account of his action he was dropped from the staff of a hospital in high standing in his community, compelled the committee to acknowledge the truth of the allegation and to find the fellow guilty as charged. However, as the fellow later admitted his indiscretion and promised to change his manner of living and also by reason of affidavits of his intimates that such an attempt was being made, the committee felt that an opportunity should be given him to rehabilitate himself, and the case was placed on file pending further complaints.

Every case heard has been settled only after the accumulation of evidence which we as a committee know would substantiate the committee's findings before a board of trial and we believe likewise, before a court of law.

WILLIAM J. BRICKLEY,
ALLEN G. RICE
FRED R. JOVETT
ARCHIBALD R. GARDNER
RALPH R. STRATTON *Chairman*

APPENDIX NO 3

SOME COMMENTS ON THE PROCEEDINGS OF THE MEETING OF THE HOUSE OF DELEGATES OF THE AMERICAN MEDICAL ASSOCIATION HELD IN CHICAGO, JUNE 7 TO JUNE 9 1943

The House of Delegates was called to order promptly at 10 a.m., Monday morning, June 7, 1943. The report of the Committee on Credentials showed that 144 delegates were present. A supplementary report given on Tuesday morning, June 8, showed that 170 members of the

House of Delegates had been registered. All states, all sections and three government services had complete registration. The only delegates not in attendance were those from Alaska, the Isthmian Canal Zone, the Philippines and Puerto Rico. This was a most remarkable record, showing the interest and sincerity of individual members. Rarely has there been shown so much interest, so much seriousness in conducting the proceedings of the House of Delegates as was shown at this meeting.

The whole atmosphere seemed to be surcharged with the importance of the business under consideration. The reference committees appointed by the Speaker were regionally well balanced. The hearings were exceptionally well attended. The attention of the Council of the Massachusetts Medical Society is especially called to the addresses of Dr. H. H. Shoulders, speaker of the House of Delegates, of President Frederick W. Rankin, of President Elect James E. Paullin, of Surgeon General Norman T. Kirl, of George M. Morris, president of the American Bar Association, of Dr. J. C. Routley, secretary of the Canadian Medical Association, and Brigadier General David N. W. Grant.

General David N. W. Grant is a flight surgeon of the United States Army. On taking over the department of flight surgeons a year and a half ago, he found that there were in the Army 97 flight surgeons. Today there are 9300 Army flight surgeons. When we consider these figures, we are greatly astonished at the amount of work accomplished by General Grant.

It would seem as if it were the bounden duty of every member of this council to read these addresses carefully. In short, terse and plain language they contain the aims, the duties and the responsibilities of the American Medical Association. The inspiring address of the Speaker of the House, Dr. H. H. Shoulders, merits special attention.

The most important subject under discussion was the proposition that the American Medical Association establish in Washington, D. C. a council on medical care. Resolutions were presented from the state medical societies of Minnesota, Indiana, New Jersey, Nebraska, Oklahoma, and Ohio, and from the Section of Radiology, supporting such a general proposition. A proposal called for a council of nine members, from nine geographic subdivisions of the United States. Among the recommendations was one proposing the establishment and maintenance in Washington, D. C., of a full time executive director, who would act as secretary of the council and whose duties would be specified by them. Another proposal suggested that such an executive director be a physician who has been actively engaged in the private practice of medicine for not less than five years during the previous ten years. Another proposal recommended that the council be further authorized to hire such legal and administrative help as it deemed necessary. Still another suggested that the Council on Medical Service submit a budget for its fiscal year to the Board of Trustees of the American Medical Association. All the resolutions asking for the establishment of a council on medical service were referred to the Committee on Legislation and Public Relations for consideration. At a stated time, this committee held a hearing on the subject. The hearing was very well attended by delegates to the session. All persons who wished to discuss the question of establishing a council on medical service were given time and ample opportunity to present their views.

The Reference Committee on Legislation and Public Relations reported as follows: All the resolutions submitted as well as the opinions expressed at the open meeting of your reference committee have been given

full, earnest consideration. There appears to be one objective in all of them."

The reference committee reported in favor of such a council. Before this report could be enacted into a law of the Association, it was necessary for the Board of Trustees to consider the matter and give its approval. The Board of Trustees met with the Committee on Public Relations and recommended the creation of a Council on Medical Service and Public Relations.

It was finally determined after conferences and certain recommendations for change of by-laws that the Council on Medical Service and Public Relations be created by the House of Delegates of the American Medical Association. It was agreed that the membership of this council shall consist of six members, selected according to geographic distributions, and the president, the immediate past-president, the secretary and a member of the Board of Trustees of the American Medical Association. Their functions shall be as follows:

The functions of the Council on Medical Service and Public Relations shall be (1) to make available facts, data and medical opinion with respect to timely and adequate rendition of medical care to the American people; (2) to inform constituent associations and component societies of proposed changes affecting medical care in the nation; (3) to inform constituent associations and component societies regarding the activities of the Council; (4) to investigate matters pertaining to the economic, social and similar aspects of medical care of all the people; (5) to study and suggest means for the distribution of the medical service to the public consistent with the principles adopted by the House of Delegates; (6) to develop and assist committees on medical service and public relations originating within the constituent associations and component societies of the American Medical Association. In the exercise of its functions this Council with the co-operation of the Board of Trustees, shall utilize the functions and personnel of the Bureau of Legal Medicine and Legislation, the Bureau of Medical Economics and the Department of Public Relations in the headquarters office.

The names of the following men were selected to act as the Council on Medical Service and Public Relations: Louis H. Bauer, chairman, Hampstead, New York; A. W. Adson, Rochester, Minnesota; John H. Fitzgibbon, Portland, Oregon; W. S. Leathers, Nashville, Tennessee; E. J. McCormick, Toledo, Ohio; James R. McVay, Kansas City, Missouri; Olin West, Chicago, Illinois; Roger I. Lee, Boston, Massachusetts; James E. Paullin, Atlanta, Georgia; and Fred W. Rankin, Washington, D. C.

Your attention should also be called to the work of the Board of Trustees of the American Medical Association. The report of the Board covers 115 pages of the handbook which is a book distributed to the members of the House of Delegates as a guide. The main report is very exhaustive. It represents a prodigious amount of work. Besides this main report there was submitted to the House of Delegates, a supplementary report entitled *Supplementary Report of Board of Trustees Dealing with Report of Proceedings of the Joint Committee Meeting of National Hospital Associations and Representatives of the Board of Trustees of the American Medical Association*.

In reading these reports there is one thing to keep in mind constantly, namely, that the House of Delegates of the American Medical Association defines the policy of the Association and the Board of Trustees carries out this

policy. It is not the purpose of your commentator to go into the details of the reports. Your commentator, however, would advise every member to read the reports and to study them carefully. The complete reports will be found in June 19, 1943, issue of the *Journal of the American Medical Association*, which also contains the report of the Council of Medical Education and Hospitals. A valued member of the latter council is Dr. Reginald Fitz, of the Massachusetts Medical Society.

One of the subjects treated by the Council of Medical Education and Hospitals is entitled "Essentials of an Acceptable School for Clinical Laboratory Technicians." Your commentator will close his comments on the accomplishment of the Board of Trustees by quoting the reference committee's remarks regarding the work of the Board of Trustees.

Your reference committee is aware of frequent criticisms of the Board of Trustees because the Board does not do this or that, and, although it should be well known by the medical profession at large, it is worth repeating that the Board of Trustees is bound by the mandates of the House and the House is responsible for the Board's activities. Your reference committee feels that the House should express its appreciation of the tremendous amount of work carried on throughout the year by the Trustees, an amount of work which has been gradually increased by the war. It recommends, therefore, that the House express its heartfelt thanks to the members of the Board for their efficient work.

Remember also, we are all members of a very large and influential nonprofit educational institution. The membership is 122,741. Its net worth is \$4,711,215.32. It has a payroll of over 500. It maintains suitable and comfortable headquarters, from which plant many publications are issued besides those of the *Journal of the American Medical Association* and *Hygeia*.

A pleasant and notable incident took place at the meeting in Chicago. A fellow-member of the Massachusetts Medical Society, Dr. Elliott P. Joslin, was honored with the bestowal of the Distinguished Service Award of the American Medical Association. The selection of Dr. Joslin as the recipient of the award gave joy and delight to every member of the Massachusetts Medical Society. The award consisted of a medal properly inscribed, which was formally presented to Dr. Joslin at the meeting of the House of Delegates on Tuesday evening, June 8. The recipients of former awards are as follows: Dr. Rudolph Matas, 1938; Dr. James B. Herrick, 1939; Dr. Chevalier Jackson, 1940; Dr. James Ewing, 1941; and Dr. Ludwig Hektoen, 1942.

The Massachusetts Delegates in attendance were as follows: David D. Scannell, Boston; Ernest L. Hunt, Worcester; Charles E. Mongan, Somerville; Walter G. Phippen, Salem; Allen G. Rice, Springfield; and Richard H. Miller, Boston. Dr. Walter G. Phippen served as a member of the Reference Committee on Medical Education. Dr. David D. Scannell served as a member of the Reference Committee on Reapportionment. Dr. Michael A. Tighe, secretary of the Massachusetts Medical Society, who was present as an observer at the meeting of the House of Delegates, was voted the privilege of attending the executive session of the House of Delegates.

Dr. Herman L. Kretschmer, of Chicago, was selected as president-elect. Dr. Kretschmer is not unfamiliar with the administration of the American Medical Association affairs as he served ten years as treasurer. He

comes well equipped assuming the responsibilities attached to the office of president elect of the American Medical Association

COMMENT

Your commentator wishes to bring the attention of the Council of the Massachusetts Medical Society to the great part that Massachusetts influence bears in the conduct of the affairs of the American Medical Association. The chairman of the Board of Trustees, Roger I. Lee, the president of the Massachusetts Medical Society is an enormous responsibility. One cannot overestimate the demands on his time and on his strength which the heavy responsibilities of his office exact. I wish to testify that I think he is one of the ablest chairmen of the Board of Trustees that the American Medical Association has ever had. There is another member of the Massachusetts Medical Society who works very quietly and very effectively. The members of the American Medical Association need never worry concerning the kind and quality of medical service and medical education which is promoted by the American Medical Association while Dr. Reginald Lutz is a member of the Council of Medical Education and Hospitals.

Last but not least is the part that Dr. Frank H. Lahey has taken in the affairs of the Procurement and Assignment Service in bringing about the enlistment of 45,000 doctors in the American armed services.

CHARLES E. MORGAN, *Senior Delegate*

APPENDIX NO. 4

REPORT OF THE MASSACHUSETTS STATE COMMITTEE OF THE PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS

On August 26 the *New England Journal of Medicine* printed an editorial called —or Else. Here in bold faced type, was stated that the armed forces need medical officers so urgently that in order to increase enrollments a directive already had gone to the commanding officers of several Service Commands authorizing them if necessary, to induct into service physicians up to forty-five years of age who had been declared available by the Procurement and Assignment Service. The editorial went on to warn physicians in this age group who had been declared available, and who had failed to offer their services, to apply for commissions at once. Unless they did this it seemed probable that they might soon be inducted into the Army as privates eventually to receive commissions of minimal rank rather than ones which took into consideration age and experience.

The justification for this editorial is now clear. The state director of Selective Service has recently informed your committee of two important directives under which he will be guided in the future. The War Manpower Commission has authorized Selective Service to induct pre-Pearl Harbor fathers after October 1, 1943 in the sequence of their order number and as fast as needed after the induction of single men and childless married men. The War Department has authorized the commanding generals of Service Commands to waive age limitations for induction in the case of physicians between the ages of thirty-eight and forty-five when they are declared available for military duty by the Procurement and Assignment Service and when waivers are requested by state directors of Selective Service.

These two statements make it plain that dependency need no longer play a part in determining Selective

Service deferments for doctors and that age, also within the limits specified can be discounted. Thus Selective Service and Procurement and Assignment now appear to have considerably stronger authority over physicians than ever before.

As a result of this the problem of the graduate of the standard school promises to be more baffling than ever. Consider as a typical illustration the City of — which happens to have a population of about 110,000 people. In it are 70 doctors born between 1879 and 1898, all too old for military service. In addition there are 2 younger men who have been declared essential and 7 who have applied for commission and have been rejected on physical grounds. These 79 men are able to cover the medical needs of this city in a satisfactory manner, but in addition there are 6 graduates of standard schools who have been declared available without doing anything about it and 14 who are licensed to practice in Massachusetts but are ineligible for commission because they are foreigners or graduates of schools not recognized by the Surgeons General.

If the men who are graduates of standard schools are reported to Selective Service they may be discriminated against in favor of men whose competency is less certain. Heretofore the latter group has been protected on the ground that any doctor with a license to practice in Massachusetts was better than none. Now that doctors are liable to induction, the situation has changed. In future to be as fair as possible your committee proposes to report to Selective Service when necessary two groups of physicians declared available: one comprising physicians who have not applied for commissions though asked to do so, and the other, physicians ineligible for commission whose services are not essential to the health and welfare of the community. If any physicians must be inducted both these categories should be subjected to equal scrutiny.

On August 26 there began what has been called the third phase of procurement. This consists in the appraisal of men under forty-five years of age who are called essential. The supposition has been made that the longer the war lasts the greater is the likelihood that a number of doctors will be inducted out of the Army or Navy and that they may be able to resume work in the various communities to which they belong. As such men return it may be possible little by little for them to replace men now held as essential.

The essential men therefore have been asked to apply for commissions and to have physical examinations by the Army or Navy so as to make it a matter of record that they are not objectors that they have applied for commissions when asked to and what the state of their physical fitness is. The directive regarding this matter says that *no such man will receive a commission until he has been declared available* by Procurement and Assignment and Procurement and Assignment has been ordered not to declare any such man available until a satisfactory replacement for him has been found.

The Corps Area chairman and the state committee have agreed to accept as definition for the word *satisfactory* that used in the *Concise Oxford Dictionary* of 1931 leaving no room for complaint causing satisfaction adequate.

A certain degree of suspicion has become manifest on the part of the essential men who so far have been approached. They appear to suspect that here is a trap to drive them into service by forcing as their replacements

physicians who cannot be called satisfactory under the definition described. Such a suspicion appears unfounded. Your committee believes that the War Manpower Commission intends to live up to its statement that no man called essential will be commissioned until he is declared available. He will not be declared available until, in fact, there has appeared to take his place, a replacement who can leave no room for complaint.

In the September 11 number of the *Journal of the American Medical Association* was described a plan which will go into effect in 1944 for the allocation of interns and residents in hospitals. Stated briefly, this plan proposes henceforward to have the internship last for nine months instead of a year, thus synchronizing it with the accelerated medical school program. Each state will be assigned a quota of interns and residents which will total about two thirds of the numbers recorded in 1940. Each hospital, also, will have an assigned quota, though in individual hospitals consideration will be given to obvious injustices which might occur with too arbitrary an application of the allocation plan. The basic principle of the plan is to devise a method of equalizing the distribution of interns and residents in our hospitals and to prevent their overconcentration in certain institutions.

That a certain number of resident and assistant resident physicians are necessary for the proper conducting of hospital services is recognized. Thus hospitals in the habit of employing resident physicians will be permitted to retain a certain number. In establishing the quotas for residents, one third of the interns beginning their services at each nine months may be retained for a second nine months' service as assistant resident physicians and half of that group may be retained for a third nine-month period to serve as residents. A man may leave one hospital at the end of his nine or eighteen months' service to go to another so that under this plan, free movement of young doctors will be encouraged within the limits of the quota for the state.

The exact details of the manner in which the plan is to operate in Massachusetts have not yet been clarified. It seems probable, however, that our large hospitals will be asked to yield approximately a third of the house staffs to which they are accustomed, and that some 75 young men will thereby become available to the small hospitals so badly needing them.

Up to the present time your committee has been more occupied with the procurement of physicians for the armed forces than in their assignment to civilian needs. The time has come, however, when the latter phase of the work has begun to receive an increasing amount of thought. Analyses have been made which serve to illustrate the present distribution of physicians in Massachusetts. The small cities and the less densely populated areas continue to be poor in physicians while the large cities still claim a relatively high concentration of medical talent. This finding is easily explainable, since areas of dense population, by necessity, are required to perform a type of medical work which requires much highly trained specialism and medical teamwork that is extremely complicated.

In spite of the number of physicians who have left practice, there so far has been very little complaint of medical shortage. Such complaints as have been received, on critical study, have depended almost invariably rather on a given physician's personal popularity with his patients than on his essentiality. There are still a

number of physicians who can be spared without detriment to civilian care.

HOWARD M. CLUTE
EDWARD L. KICKHAM
DWIGHT O'HARA
WALTER H. PULSIFER
B. P. SWEENEY
REGINALD FITZ, *Chairman*

APPENDIX NO. 5

REPORT OF THE WAR PARTICIPATION COMMITTEE

The first part of this report is one of progress. On May 24, 1943, the Council passed the following resolution:

WHEREAS, the War Manpower Commission has announced that there is immediate need for more physicians to serve as medical officers in the armed forces of the United States; and

WHEREAS, the War Manpower Commission has announced that Massachusetts should supply more medical officers than have so far been commissioned from the state; and

WHEREAS, a plan has been suggested by the War Manpower Commission through which the enrollment of medical officers may be accelerated with the help of county or district medical societies in certain states; therefore be it

RESOLVED, that Reviewing Committees be established by each District Society, the members of which shall be nominated by the District Society Presidents and appointed by the President of the Massachusetts Medical Society. Such committees shall serve for the general purposes outlined in this report.

Promptly on the appointment of the district reviewing committees by the President, the names of Massachusetts physicians considered available for military service by the State Committee on Procurement and Assignment were sent by this committee to the proper district committees together with pertinent information concerning each. The decision on each man by the local committees was thereupon sent to the State Committee on Procurement and Assignment. The work of the reviewing committees was in most instances conscientiously carried out. Much credit is due these men, and this has been duly bestowed by your chairman on the direction of the committee at its meeting of September 22, 1943, by letters containing a general report and an appreciation of their prompt and conscientious action.

The figures to date are as follows:

Names submitted to the Reviewing Committees	321
Names have been reported (23 outstanding)...	298
Available	102
Already in service.....	31
Application for commission already submitted	32
Essential	29
Not available.....	104
Graduate substandard school..	21
Sociologic reasons.	17
Rejected by Army.....	14
Unable to locate by mail or phone	16
Over 45 years old.....	5

Not a citizen	7
Osteopath	6
Moved out of state	8
Intern	1
Refused to apply	2
Dead	1
Out on bail	1
No reason given	5

In accordance with instructions from the committee at its meeting on July 28, 1943, your chairman requested in writing from Dr. Reginald Fitz, state chairman of Procurement and Assignment, an appraisal of the results of the activities of the reviewing committees. Dr. Fitz was not able to be more specific than is indicated in the following paragraphs of his reply.

A number of men by the time they were asked to appear for review had already applied for commissions and several had already gone into uniform and left. Happenings of this sort were inevitable because the names of men referred to the reviewing committees were already declared available, and many had accepted their classification somewhat slowly, but nevertheless surely. A second factor that has made the work of the reviewing committees difficult to analyze is that since all the names submitted had been declared available, the Army or Navy were applying pressure on many of the men at the same time as they were reviewed by the committees. The combination of all this pressure, however, has seemed to yield results, for both Army and Navy procurement offices inform me that the stream of applicants continues, although neither service can state with any assurance that there has been any sharp rise in the number of applicants since the reviewing committees were established. I repeat, however, that these committees have been helpful. It seems to me that their chief contribution has been to let a reluctant doctor in any community know that a larger group than the Procurement and Assignment Service, plus the Army or Navy recruiting offices realize that he has been declared available. This fact in itself has tended to stir up a favorable opinion toward making doctors take the word available more seriously than heretofore. To this must be added the constant appeal in medical journals and newspapers of the need for more medical officers in the large scale offensive which seems steadily more imminent.

A complete copy of this letter was forwarded to the chairman of each local committee along with the above mentioned word of appreciation.

The plan of the staff of the Beth Israel Hospital to care for the practice of those of their number who have entered the United States Service was referred to this committee and came under discussion at its meeting of July 28, 1943. The committee expressed its sympathy with the ideology involved but did not recommend approval by the Society of the plan as outlined in the protocol.

* * *

The second part of this report concerns itself with the future functions of the Committee on War Participation. In a letter from Walter F. Donaldson, chairman of the National Committee on War Participation of the American Medical Association, various possible functions were considered, ranging from the sending of remembrances to fellow members in the services to active co-

operation with Civilian Defense organizations in each community.

Your committee considered carefully each of these suggestions and noted that the Massachusetts Medical Society is attacking many of the important problems posed in already organized committees, such as the Committee on Industrial Health, the Committee to Aid the District Rationing Administrator, and the Committee concerned with Prepayment Medical-Care Costs Insurance.

At our last meeting on September 22, 1943, there was much discussion as to what the committee should properly interest itself in now that the bulk of the reviewing has been completed. Many possible functions were considered, the most important being that of relocation of physicians to meet local community needs. It seemed to us that this and other complicated matters needed more consideration before a definite approach to them could be made—also that the influence of the committee should be broadened and decentralized so as to be more effective in local matters.

We, therefore, recommend that the present reviewing committees in the several Districts be not discharged, but be retained with the same personnel and organization (chairmen and secretaries) as district committees on war participation, subcommittees, so to speak, of this committee. We also recommend that an appropriation of \$300 be made to this committee for past and future expenses, largely clerical, from the time of its appointment to January 1, 1944.

CARL BEARSE
REGINALD FITZ
DWIGHT O'HARA

WILLIAM B. BREED, *Chairman*
RALPH R. STRATTON, *Co. Chairman*
MICHAEL A. TIGHE, *Secretary*

APPENDIX NO. 6

REPORT OF PROGRESS BY THE POSTWAR LOAN FUND COMMITTEE

The Postwar Loan Fund Committee was organized on June 16, 1943, with fifteen members appointed by the president, Dr. Roger I. Lee.

The second meeting of the committee of the whole was held on Wednesday, August 11, 1943, at 8 Fenway, at which time the reports of the five subcommittees appointed by the chairman to study certain phases of this problem were read by the chairman of each subcommittee and discussed by all members of the committee of the whole. This is a report of progress of the committee of the whole.

The first subcommittee (Dr. Pierce H. Leavitt, chairman) studied the following questions:

- (1) Amount of loan to be granted
- (2) Whether or not interest is to be charged
- (3) Whether or not endorsers will be necessary
- (4) Length of time the loan may run

The committee reported that it believes that the amount must, of course, be uncertain, but would depend on two factors: the amount of money raised by the Society and the need of the applicant. The committee expressed the opinion that just enough interest to remind the applicant that he had a loan and to cover the carrying charge should be collected—this interest not to exceed 2 per cent. The committee stated that in its opinion no endorsers

should be asked from members of the Society, and further stated that the length of time the loan may run should be within a two-year period. The committee of the whole, after discussing this subcommittee's report, accepted these conclusions.

The second subcommittee (Dr. Walter G. Phippen, chairman) then reported on the question studied by them:

- (1) Eligibility of persons to borrow money from the fund.
- (2) Whether or not physicians other than members of the Massachusetts Medical Society at the time of entering the armed services should be permitted to borrow from the fund.

The committee reported that it believed that only men who were members of the Massachusetts Medical Society when they entered the armed forces should be permitted to borrow from the fund. None of the members believed that the fund should be open to all physicians in Massachusetts. The committee of the whole discussed this report, and it was approved in principle.

The third subcommittee (Dr. Charles Wilinsky, chairman) considered the question whether the fund should be raised by:

- (1) Increasing dues.
- (2) Assessing members \$10 or more for one year.
- (3) Assessing members \$10 or more over a period of three to five years.

The committee reported as follows:

It is our considered opinion that these funds should be raised not by increasing the dues, but rather by an annual assessment of \$10 for the duration of the war, unless otherwise modified by future action of the Council.

The committee reported that the present by-laws of the Society make provision for such assessments and authorize the Treasurer to collect them. The report of this subcommittee was considered at great length by the committee of the whole, and the report was accepted in principle.

The fourth subcommittee (Dr. Herbert L. Lombard, chairman) reported on how best to inform the members of the Society in the armed forces of the availability of this fund. The committee reported as follows:

We unanimously agree on three points:

Information should be printed in the *New England Journal of Medicine*. There should also appear in a box on the cover of the *Journal* an announcement calling the article on the inside page to the attention of members.

Form letters should be sent to men in the armed services notifying them of this action by the Society.

Form letters should be sent to other members of the Society with the annual bills for dues, stating the availability of these loans.

This report was also accepted in principle by the committee of the whole after considerable discussion.

The fifth subcommittee (Dr. George Leonard Schadt, chairman) made a report on the question concerning the relation of the individual county district societies to the Society in developing and making the Postwar Loan

Fund workable. The subcommittee believed that the fund should be administered from the headquarters of the Massachusetts Medical Society, rather than from the district societies; so that no member would be embarrassed in going to his district society and asking for a loan. It was also thought that a member desiring a loan would be more apt to ask for it if it were done through the headquarters of the Society. This question was also discussed at length and agreed to in principle by the committee of the whole.

GEORGE LEONARD SCHAT, *Chairman*

APPENDIX NO. 7

MASSACHUSETTS MEDICAL SERVICE REPORT

This presentation is an informal report of progress to bring you information concerning the present status of Massachusetts Medical Service. Your corporation has been satisfactorily established, and active enrollment of subscribers is proceeding. Doubtless you have noted the excellent publicity procured for the Blue Shield by our Blue Cross associates, as they celebrated their own sixth birthday recently.

ENROLLMENT FIGURES

At the time of the last report in June, there was an enrollment of only about 2000 subscribers in the Blue Shield. This represented the culmination of six months' effort in which most of the work was preliminary ground breaking efforts in the industries. As a consequence of this preliminary groundwork, recent months have witnessed an increasing enrollment which promises a total subscription of about 10,000 members at the completion of our first year in January, 1944. Under the present arrangement with Blue Cross, each salesman is held responsible for a quota of 200 Blue Shield subscribers as a monthly average. The Blue Cross quota for each salesman is 500 subscriptions. The possible enrollments on this basis are 13,000 at the end of the first year. Our experience to date indicates that we may fall somewhat short of this objective—10,000 or somewhat over it, depending on prospective enrollments in one large company.

This first year experience compares favorably with the results obtained in other states with the exception of Michigan. However, the results obtained in Michigan must be regarded as anomalous and not related to the realities of experience in the bulk of the states where there are no massive industrial units ready to supply subscribers in the mass of 100,000 or over. It appears safe to assume now that the industrial pattern in Michigan is unique, and is largely responsible for the rapid expansion of Michigan Medical Service, and that no other state medical organizations are likely to encounter a pattern which will assure any such result. A state such as Massachusetts with a myriad of small or moderate-sized industrial units is going to encounter hard digging and slower growth. With reference to other states having medical society prepayment programs, Colorado enrolled somewhat less than 10,000 in the first year, but feels that further expansion is impeded by the fact that it cannot, under the law, sell the overincome group, as the Massachusetts Medical Service is empowered to do; Pennsylvania in about three years has enrolled approximately 10,000 subscribers; New Jersey with a complete hospital medical-surgical contract has enrolled somewhat less than 10,000 subscribers. This last result may indicate, from

our contrasting experience, that complete hospital coverage is not necessarily more attractive to the subscribing public than a surgical-obstetric contract such as Massachusetts offers. Significantly, no major group is now offering to the public a complete comprehensive medical care contract in and out of the hospital, as its basic policy.

ENROLLMENT PRACTICES

A brief statement regarding enrollment practices should be made because of its important bearing on the rate of growth of our corporation. Sale of contract, as in Blue Cross, is of necessity offered to groups of persons previously organized for nonmedical reasons. The practice is to require a certain percentage of any group to enroll before their acceptance as a subscribing group. The average requirement in the several state plans is 50 per cent of any group. Michigan requires 75 per cent. At a recent meeting of the medical service plans, an effort was made to extract the rationale for such high requirements from the various groups. There seemed to be no satisfactory account from any group for their percentage requirements. It actually appears possible that Michigan's 75 per cent rate (an impossibly restrictive requirement in most states) was imposed to delay enrollments until administrative problems were resolved. A second important observation was that all executives, when directly questioned, felt that some relaxation from rigid requirements could be made with reference to seasoning of a group by prior subscription to Blue Cross or a commercial carrier. However there were no specific recommendations, and suggestions relative to seasoning of groups was distinctly nebulous.

Consideration of these two facts led to our liberalization of Blue Shield enrollment requirements in Massachusetts with reference to seasoning of a group by a prior Blue Cross subscription. There was a large body of potential subscribers to Blue Shield (500,000) who were seasoned to varying extents (one to five years) by prior Blue Cross contracts. The experience of Blue Cross with regard to stabilization of the exposure in a given group is that after three years the hospital utilization, as measured by the loss ratio, can be fairly accurately measured. Loss ratio means the number of cents out of each dollar paid in as premiums by the insuring group, which has to be paid out for hospital care in a given year. The loss ratio was quite variable from group to group. It varied from a favorable figure of 60 cents or less in a group showing an acceptable rate of hospitalization, to 80 cents or more in a group with an excessive utilization record. Satisfactory seasoning or stabilization of a group was not achieved until after three years of insurance. Two important factors which influenced the loss ratio figure of a given group were the average health of the group, and the cultural level of the group. The lower the health standard or the higher the cultural level of a group, the higher the rate of utilization of a contract, and the higher the loss ratio (cents out of a dollar paid for hospital costs). The reverse also held true, the higher the health standard or the lower the cultural level, the lower the loss ratio, and the more satisfactory the financial experience with the group. With all these factors (seasoning, loss ratio, health and cultural levels) rationally synthesized it seemed reasonable to adjust the percentage requirements for enrollment according to the prospective experience with a given group. Our completely satisfactory financial experience to date seems to indicate the

basic soundness of assumptions derived from the above considerations. Following are the assumptions:

- (1) Any group seasoned by Blue Cross for a three year period or over, and having a satisfactory experience is indicated by a loss ratio of not over 75 per cent, may be accepted on any percentage basis.
- (2) Any group seasoned for two years with a loss ratio of not over 75 per cent, may with due consideration of health and cultural levels be enrolled on a 20 to 30 per cent basis.
- (3) Any group seasoned for eighteen months with a loss ratio of not over 80 per cent may, with due consideration of health and cultural levels, be enrolled on a 40 per cent basis. If a group is deficient in any respect, the requirement should be 50 per cent.
- (4) Failure to procure an adequate percentage in any industrial group could be safely circumvented if 75 per cent of the active Blue Cross subscribers sought enrollment.
- (5) Any large industrial group (over 500 workers) that is enrolled as a new group will be enrolled on the same base as for Blue Cross (50 per cent) unless there are sound actuarial reasons for reliving the requirements.
- (6) With seasoned small groups (less than 10 persons) whether or not a satisfactory percentage participation is procured, will be left to the experienced judgment of Blue Cross executives who are familiar with the group as a risk.

FINANCIAL STATUS

Two sets of figures outlining our relative financial status are presented. The first figures represent an estimate at the end of the first six months' period, when subscriptions had not increased significantly, the second set of figures represent what should be our estimated status after the first year is completed in January, 1944, with a probable subscription list of 10,000. These figures indicate that by January we will be operating satisfactorily in the black. We shall have met the 25 per cent reserve requirement of the Commissioner of Insurance, we shall have ample reserves to take up the second year's load of obstetrics and tonsillectomy in children due on all contracts in force for one year, we shall (with an actual loss ratio of 25 per cent and an estimated loss ratio of 35 per cent) establish a condition wherein during the second year we can retire the carried-over organizational expense of \$4000, and create a reserve which will lead toward increasing benefits. On this basis none of the \$25,000 so generously voted by the Council will have been used. Furthermore, with this satisfactory background all payments to the physicians for services rendered under the contract will have been made in full as per the agreed fee schedule. This gives Massachusetts the unique experience of organizing, establishing and operating for its first year a prepaid medical-care program and doing it completely on the black side of the ledger, with unquestionably ample reserves in the process of building. These experiences are significant for those state groups which cannot safely anticipate the huge enrollments of Michigan Medical Service. These results have guaranteed to us the continued full support of the medical profession, without evidence of significant dissension, and the friendliest and most

effective working relations with the Blue Cross group. It bears out the assumption that a 10,000 subscription list carried on the basis of adequate premium rates, and

TABLE 1. *Profit and Loss Statement of Massachusetts Medical Service for the Period Ending July 31, 1943.*

Farned subscriber payments	\$6,833.26	
Surgical expenses		
Payments made to or provided for doctors	\$2,995 00	
Operating expenses		
Printing and stationery	\$3,279.94	
Books, newspapers and periodicals	687.25	
Publicity	529.41	
Insurance and bonding	200.00	
Conference expense	192 96	
Home office travel	117.36	
Dues and subscriptions	25 00	
Miscellaneous	7 25	
Expenses paid by Massachusetts Hospital Service, Inc. (1943)	3,275 60	
		8,314.77
Total expenses		11,309.77
Net loss		\$4,476.51

proper working relation with the Blue Cross group, can definitely finance itself toward future expansion.

Table 1 gives the figures of a profit-and-loss statement as estimated for July 31, 1943. The earnings from premiums on sold subscriptions was \$6833.26. The total of

TABLE 2. *Estimated Financial Status of Massachusetts Medical Service as of January, 1944.*

Estimated income	\$30,000
Operating expense	\$11,000
Payments to doctors	10,000
Premium tax (1 per cent)	300
Total estimated expense	\$21,300
Reserve requirement (25 per cent)	7,500
Total estimated financial requirements	\$28,800
BALANCED STATEMENT	
Income—Expense	\$30,000 28,800
Balance	\$1,200
Organizational deficit on books	\$4,476 51
Surplus (if reserve not applicable till 1944)	\$8,700

payments to doctors and operating expenses was \$11,309.77. The net loss was \$4476.51, or but little more than the initial expense for organization, which has been carried forward on the books to be paid off when our reserves accumulate. This means that in this very early period with restricted sales and large nonrecurring expenses the

books balanced themselves except for the early organizational expense that is being carried along.

Table 2 attempts to estimate our probable status as of January, 1944, when it appears certain our enrollment will exceed 10,000 subscribers. The total income should be \$30,000. The total financial outlay for operating expenses, payments to doctors, tax premium and the reserve requirement of 25 per cent should be about \$28,800. This would leave a balance of \$1200 (but still carrying the organizational cost of over \$4000 on the books). This means that very soon in the following year this initial cost can be retired, and a reserve created. When our cost for tonsillectomies and obstetrics in the second year is measured, and when the reserve for late reported cases can be determined and established, then we can accurately find out the rate of accumulation of a reserve and plan safely for our second contract of complete medical care in the hospital.

Below is a figure of \$8700, which may represent our available reserve (exclusive of organizational costs) if, as implied by the Insurance Department, we may not be required to set up the 25 per cent reserve until the second year of operation. Under such circumstances we could now retire our outstanding organizational expense and have an estimated surplus at the first of the year of nearly \$5000.

With reference to the loss ratio (the number of cents out of each dollar paid in as premiums by the insuring group, which has to be paid out for hospital care in a given year), it is running at present at the low figure of 25 per cent, with an estimated real loss ratio on receipt of slow reports of 35 per cent. This will rise in the second year when the cost of obstetrics and tonsillectomy care in children has to be met.

Our mid-year cost of administration is 50 per cent, and with the accumulation of premiums and dilution of nonrecurrent initial expenses should drop to about 15 or 20 per cent for the year. With a combined loss ratio and running expense of only 48 to 53 per cent out of a possible 100 per cent, we are in an excellent position to absorb the second year cost of obstetrics and tonsillectomies, and create a reserve to meet our obligation of providing complete hospital medical-care protection at the earliest feasible date.

For this hopeful outlook we are indebted to the profession for its kind support, and its confidence that our initial approach to the eventually complete program is sound; and to the co-operative support and sympathy of the Blue Cross organization which, by contractual arrangement, is handling the sales and administrative end of our project. The patience and forbearance of both groups have spared us many difficult problems which have arisen in other sections of the country. For this we may be properly grateful.

NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-SECOND
ANNUAL MEETING

May 11, 1943

THE scientific session of the New Hampshire Medical Society was opened at the Hotel Carpenter, Manchester, at nine thirty o'clock in the morning, with President Timothy F Rock presiding.

The first paper of the morning was one by Drs John P Bowler and Scott Pedley, of Hanover, on the subject, "Carcinoma of the Prostate and its Endocrine Relationships". The next paper was by Dr Oliver Cope of Boston, being entitled "The Treatment of Burns". The last paper of the morning was by Dr Roger I Lee, of Boston, on "Geriatrics. The medical care of the elderly".

The afternoon session convened at two o'clock with President Rock presiding.

Dr Leonard B Morrill, of Centre Harbor, was awarded a gold medal for membership of fifty years in the Society, he spoke as follows:

I want to thank you for this medal and for the most wonderful association in the world—the New Hampshire Medical Society. Thank you very much.

Dr James W Jameson, of Concord, was presented as president elect, and spoke as follows:

I wish to express my gratitude and appreciation for this honor, and I can assure you that I will do what I can for the interests of the New Hampshire Medical Society, and also for the medical profession in the State of New Hampshire.

Dr Samuel T Ladd then presented the report of the Trustees.

FINANCIAL REPORT OF THE TRUSTEES OF THE NEW HAMPSHIRE MEDICAL SOCIETY FOR THE YEAR ENDING DECEMBER 31, 1942

<i>Receipts</i>	
Interest on various deposits, other than Benevolence Fund	\$202.09
<i>Expenditures</i>	
Expenses of Society as voted	1,100.00
Pray and Burnham prizes	150.00
Total expenditures	\$1,250.00
Decrease in funds, other than Benevolence Fund	1,047.91

GENERAL FUND

Deposits New Hampshire Savings Bank	\$3,771.97
Portsmouth Trust and Guarantee Company	2,083.41
Nashua Trust Company	225.44
United States Defense Bonds Series G	3,000.00
	<u>\$9,080.82</u>

BARTLETT FUND

Deposits Portsmouth Savings Bank (\$352.11 of this is a permanent fund, the income to be expended only for the benefit of medical science, as may be directed by vote of this society)	\$2,784.23
United States Defense Bonds, Series G	2,000.00
	<u>\$4,784.23</u>

PRAY FUND

Deposits Strafford Savings Bank (\$1000 of this is a permanent fund, the income to be expended only for prize essays)	\$229.91
United States Defense Bonds, Series G	1,000.00
	<u>\$1,229.91</u>

BURNHAM FUND

Deposits New Hampshire Savings Bank (\$1140 of this is a permanent fund, the income to be expended only for prize essays)	\$1,099.82
United States Defense Bonds, Series G	1,000.00
	<u>\$2,099.82</u>

BENEVOLENCE FUND

Deposits New Hampshire Savings Bank (\$394.50 of this is accrued income available for the purposes of the fund)	\$2,032.19
United States Defense Bonds, Series G	3,000.00
	<u>\$5,032.19</u>

A prize of \$100 was awarded for a paper entitled

Pathology, Clinical Manifestations and Treatment of Lesions of the Intervertebral Disks by 'R Thritus, pseudonym for Dr Albert Oppenheimer, of Laconia, and also a prize of \$50 for a paper entitled 'A Summarizing Review of Coexisting Intrauterine and Extrauterine Pregnancies, with a Report of One Original Case' by 'Bruce King, pseudonym for Dr Samuel J King of Farmington.

It is expected that a prize will be offered in 1943-1944, and notice will be sent to members of the Society in due course.

Correction of Trustees Report of 1942 The fifth set of figures at the right hand edge in this report should read \$782.88 instead of '\$782.78'.

The accounts of the Treasurer have been examined and found correctly cast and properly vouched.

SAMUEL T LADD
CLARENCE O COBURN
FREDERIC P LORD

The first paper of the afternoon session was entitled "Civilian Medical Defense and its Adaptation to Pericetum Civil Life," by Dr A William Reggio, of Boston.

The meeting was concluded by a paper, "Female Sex Hormone Therapy," by Dr George Van S Smith of Boston.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 29471

PRESENTATION OF CASE

A seventeen-year-old housewife entered the hospital because of pain and swelling of the dorsum of the right hand.

About four months before entry, two weeks after hitting her hand on a door casing, the patient noticed swelling and aching in the dorsum of the right hand in the region of the distal portion of the middle metacarpal bone. The swelling increased until it was the size of a small walnut. The pain varied but often the throbbing and ache involved the entire hand, elbow and shoulder. About two months before admission she was seen by her family physician who incised the mass but was unable to obtain any pus. The incision apparently healed but the lesion increased in size, at first rapidly, but later slowly.

An x-ray film of the right hand about three weeks prior to entry showed a destructive lesion measuring 3.5 by 2 cm. in the distal portion of the third metacarpal (Fig. 1). This appeared to destroy and expand the shaft of the bone and to extend to the head of the metacarpal. In the anteroposterior view, the outlines appeared clear; but in the lateral view the outlines were not definite. Fine trabeculae were seen through the lesion, and there was a small amount of periosteal reaction along the anterior and lateral aspects of the shaft. The patient had lost 17 pounds during the preceding two months. There was no fever, swelling in the elbow or pain in the other bones, joints or muscles. Her general health had otherwise been excellent.

Physical examination showed a well-developed and well-nourished girl in no distress. Examination of the heart, lungs and abdomen was negative. Over the dorsum of the right hand was a hard, nontender mass, about 5 cm. in diameter, firmly attached to the underlying structures, but not to the overlying skin. The mass was situated near the head of the middle metacarpal bone.

The extensor tendons were apparently not involved.

The blood pressure was 112 systolic, 70 diastolic. The temperature was 99.6°F., the pulse 86, and the respirations 22.

Examination of the blood showed a red-cell count of 4,060,000, with 80 per cent hemoglobin. The white-cell count was 9300, with 73 per cent neutrophils. A blood Hinton test was negative. The blood calcium was 10.9 mg. per 100 cc., the phosphorus 3.6 mg., the phosphatase 4.6 Bodansky units. A repeat x-ray examination, three weeks after the first one, showed a definite increase in the size of the lesion. The majority of the bony trabeculations had disappeared. No evidence of metastases was seen in the chest.

On the fourth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CHANNING C. SIMMONS: We have here a young woman with a painful tumor in the back of the hand following trauma. I assume that the x-ray films of the other bones and of the chest were negative. According to these x-ray films the tumor is in the distal end of the third middle metacarpal bone. It is expansile with a relatively sharply marked outline and with some periosteitis, but at the point where it joins the shaft, the bone has a moth-eaten appearance.

We have as usual the same three general groups of conditions as possibilities for diagnosis: first, an inflammatory condition, such as syphilis, tuberculosis, osteomyelitis or sarcoid; second, a generalized bone disease, such as osteitis fibrosa, fibrous dysplasia or one of many others—a congenital or possibly traumatic condition; and third, a tumor either primary, benign or malignant, or metastatic.

I shall assume from the history and the blood and physical examinations that the patient had no generalized bone disease such as osteitis fibrosa cystica. Presumably this was not congenital because she had no previous history of deformity of any sort. If it were due to trauma one would expect a history of swelling and pain that diminished in time and did not recur. In regard to tumor, there is no evidence so far as I can see of a primary malignant focus in this woman. It is true that metastases are likely to take place at a point on the body that has been traumatized. Presumably a hematoma following the trauma makes a good bed in which the metastatic cells may grow. Primary malignant tumors of the phalanges are almost unknown, and tumors of the metacarpal bones are rare.

*On leave of absence

The common benign tumors in this situation are chondroma and giant cell tumor. A benign tumor unless complicated by fracture is rarely painful, a malignant tumor is painful. One would expect that a benign tumor of the chondroma type

My diagnosis is either giant cell tumor or chondroma, with fracture, which would cause pain, or, possibly, a malignant tumor of the metacarpal bone, either osteogenic or Ewing's sarcoma. I do not see how a definite diagnosis could have

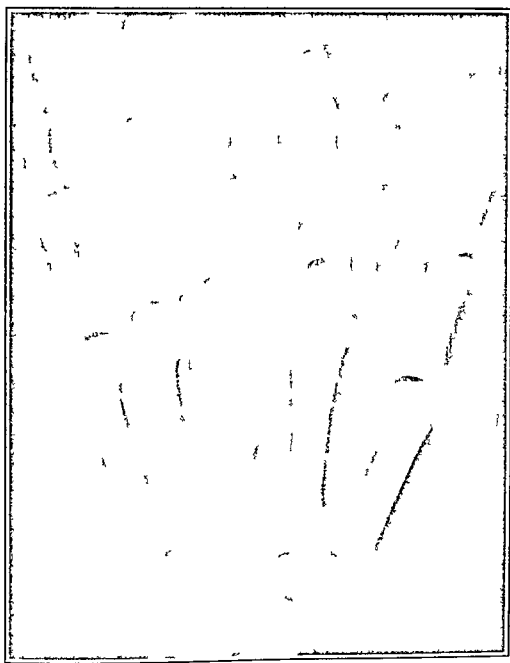


FIGURE 1 Roentgenogram of Hand

would be more clear cut in the x ray film and would not present a moth eaten appearance of the shaft. The same remark is true for giant cell tumor. A malignant tumor, osteogenic sarcoma, in this site is rare, as is also Ewing's sarcoma. I have seen both these tumors in metacarpal bones, but the x ray films in this case are not characteristic of either of them. The films of a giant-cell tumor may closely resemble those of a giant-cell tumor. In one such case, presented at a conference last winter, the lesion was located at the lower end of the fibula. Osteogenic sarcoma cannot be excluded. With an essentially normal temperature and white cell count, there was obviously no inflammation. The fact that the physician did not obtain pus when he operated is a further indication that it was not inflammatory

been made without a biopsy. The physical examination is incomplete, and no mention is made of pigmented areas in the skin.

DR BENJAMIN CASTLEMAN: None were found.

DR MILFORD SCHULZ: One wonders about the change in character of the lesion, and the fact that the shaft seems to project into the tumor mass. I think that that was described by Dr E. A. Codman in giant cell tumors, was it not?

DR SIMMONS: Yes, but they usually have a clean cut saucer shaped depression where the tumor joins the medulla. Pain unrelieved by rest is suggestive of either an inflammatory condition, fracture or a malignant tumor.

DR SCHULZ: The point was raised about malignant degeneration of a chondroma because of the change between the two x ray examinations.

DR ERNEST M. DALAND: Dr Codman has described this appearance and it has been present

in a number of cases that I have operated on. There usually is a saucer-shaped depression in the shaft proximal to the lesion, which is quite characteristic of giant-cell tumor.

DR. CASTLEMAN: Is that present in this case?

DR. SCHULZ: Yes, but it is exaggerated.

DR. SIMMONS: The point is that the shaft is usually not moth-eaten.

DR. SCHULZ: Could that not be due to the fact that we are looking at it tangentially. I do not see it in the lateral view.

DR. CASTLEMAN: What would you do about this, Dr. Simmons?

DR. SIMMONS: I should explore the tumor.

DR. CASTLEMAN: Would you do a biopsy, or take it all out?

DR. SIMMONS: That depends on what was found. If it were a benign tumor, I should be inclined to remove all the bone and amputate the finger. I do not believe that excision of a tumor as large as this will give a good functional result in later life.

CLINICAL DIAGNOSIS

Chondroma of metacarpal bone?

DR. SIMMONS'S DIAGNOSIS

Benign giant-cell tumor or chondroma.

ANATOMICAL DIAGNOSIS

Benign giant-cell tumor.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The surgeon removed the upper four fifths of the metacarpal bone. The finger was not amputated. When opened the lesion proved to be a benign giant-cell tumor filled with hemorrhagic yellowish material and fluid blood.

DR. WALTER BAUER: Benign?

DR. CASTLEMAN: Yes. The stroma was a little more active than that of the average giant-cell tumor. It might be classified Grade II according to Jaffe's grading.* In this group there is some tendency to recur and therefore resection of the tumor rather than curettage is the treatment of choice.

CASE 29472

PRESENTATION OF CASE

An eighteen-year-old schoolgirl entered the hospital because of pain in the right knee of two weeks' duration.

*Jaffe, H. L., Lichtenstein, L., and Portis, R. B. Giant cell tumor of bone: its pathologic appearance, gradings, supposed variants and treatment. *Arch. Path.* 30:993-1031, 1940

Two weeks before entry, four days after having been horseback riding, the patient noticed slight swelling and pain in the medial aspect of the right knee and exaggerated pain on full flexion. The pain kept her partially awake for several nights. A few days before entry x-ray films taken at an outside hospital were said to have shown a shadow in the right knee. The symptoms regressed and for the week prior to admission she was asymptomatic. There was no fever, chills, sore throat, pain in other joints, muscles or bones or other history of trauma.

No history of childhood diseases was obtained, but the patient was said to have had "growing pains" in her legs.

Physical examination showed a well-developed and well-nourished girl. There was a questionable slight thickening around the medial aspect of the right knee, without any limitation of motion or tenderness. No other abnormal findings were present.

The blood pressure was 120 systolic, 80 diastolic. The temperature was 98.2°F., the pulse 60, and the respirations 16.

Examination of the blood showed a red-cell count of 4,020,000, with a hemoglobin of 13.8 gm., and a white-cell count of 7100, with 64 per cent neutrophils. The urine was negative. The blood sedimentation rate was normal. A blood Hinton test was negative.

X-ray examination of the knee showed a 5-by-2.5-by-2.5-cm. area of rarefaction in the posteromedial portion of the lower shaft of the right femur just above the internal condyle (Fig. 1). Its margins were sharply defined and rather dense. There was a small amount of dense periosteal proliferation over it. No definite soft-tissue mass was seen. The remainder of the bone displayed slight decalcification. The skull, hands, feet and the right humerus were normal. There was slight decalcification of the bones of the right foot. The blood calcium was 12 mg. per 100 cc., the phosphorus 4.7 mg., and the phosphatase 2.7 Bodansky units. One observer noted two areas of brown pigmentation over the left thigh and one on the right shoulder.

On the third hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ERNEST M. DALAND: The physical examination and the history seem to be entirely negative. The laboratory examination is essentially negative, except for slight elevation of the blood calcium. The problem comes down to one of interpretation of the x-ray findings. We have here an oval-shaped defect above the epiphyseal line that extends

down quite close to the epiphyseal line. This is not a central lesion. It is medial and posterior. It does not extend all the way through. In one view there is no expansion of the bone, and in another there is expansion or perhaps periosteal

myelitis or a Brodie's abscess is that it did not involve the medulla. We can also rule out a giant cell tumor. Giant cell tumors in the femur are much likelier to be in the condyle extending down to or close to the articular surface. A giant-



FIGURE 1. *Lateral and Anteroposterior Roentgenograms of Knee*

proliferation; but we are not dealing here with an expansile type of tumor. The x-ray interpretation points out also that the margins are sharply defined and rather dense, which gives one the impression of something going on for some time and well walled off from the rest of the bone. No soft-tissue mass was felt, which is important because it helps us rule out a malignant lesion, particularly a primary malignant lesion, such as an osteogenic sarcoma. The skull, hands, feet and so forth were normal. They were checking to see if the patient had other cysts of the same sort. The note is made about slight decalcification of this bone and also the bones of the right foot. I am not impressed with the decalcification in the bones that I see, although I have not seen the x-ray films of the foot. Two weeks' disability is hardly time for decalcification from loss of use.

The differential diagnosis comes down to the decision whether we are dealing with a benign tumor, an inflammatory condition or a malignant tumor. I think we can rule out acute osteomyelitis because of the lack of fever, elevated white cell count and definite localized tenderness. A lesion of this size due to osteomyelitis would probably have given symptoms much sooner than two weeks ago. Another point against osteo-

cell tumor in this region is usually central, expansile and spherical—that is, the transverse and perpendicular diameters are about equal. I think that we can also rule out a primary malignant tumor. The lesion does not have the appearance of an osteogenic sarcoma. The sharp line of walling off and absence of soft-tissue mass are the two cardinal points in favor of a benign condition. The blood chemistry helps us rule out hyperparathyroid disease, and also we can rule it out on the basis that this was a solitary lesion with a sharp line of demarcation, whereas in hyperparathyroidism we should expect it to fade out slightly.

The three possibilities are a solitary cyst, osteitis fibrosa cystica disseminata, the syndrome that Dr. Fuller Albright¹ described, or a chondroma. In the syndrome spoken of as Albright's disease we should ordinarily expect to have multiple lesions, although that is not absolutely essential. The phosphatase is usually elevated and I suspect that the phosphatase is elevated according to the number of lesions and the activity of the lesions. Here we have a normal phosphatase, with only one lesion. We have the statement that one observer noted two areas of brown pigmentation over the left thigh and one on the right shoulder.

DR. BENJAMIN CASTLEMAN: That observer was Dr. Albright.

DR. DALAND: Dr. Albright must have been surprised to find them on the opposite side of the body, because usually these pigmented areas are on the same side as the lesion. I am a little skeptical about these lesions anyway. I believe that they can be found in most patients if one looks for them. We have no description of their size. A few years ago at the Memorial Hospital in New York someone was interested in melanomas and undertook to see if it would be possible to remove pigmented areas in all patients who came into the clinic. The first one hundred patients averaged 20 brown spots apiece, so that the three areas in this case do not impress me much. In Albright's syndrome, patients are apt to have disordered catamenia. There is no note here that there was any. I believe we can rule out that syndrome because these pigmented marks were not definite. The phosphatase was normal. The pigmented lesions were not on the same side, and there was only one bone lesion.

Putting aside that syndrome, we then come to the old diagnosis of solitary bone cyst. As Dr. Richard Schatzki has pointed out here, these solitary cysts when opened may not contain a fluid material. It may be semisolid material and perhaps the term solitary cyst is not a good one.

The last possibility is that this patient had a chondroma. A benign cartilaginous tumor usually occurs somewhere near the epiphyseal line. I think this is near enough to fall within that category. They develop in places where there has been cartilage previously, and that is true at the epiphyseal line. Another characteristic of a chondroma is that it may get to be fairly large before it gives any symptoms. It may be that it is the periosteal proliferation, where the tumor has bulged slightly, that produces the symptoms. With a chondroma we ought to have a sharp line of demarcation, such as we have here, and that is what I believe was found at operation.

DR. FULLER ALBRIGHT: A few weeks ago we had a case somewhat similar to this which I diagnosed (correctly, for once) as neurofibromatosis, and I pointed out at that time that any cyst-like appearance at the lower end of the femur might be neurofibromatosis as this is a favorite site for such lesions. So when I saw this case shortly after that conference, that diagnosis was strongly considered. I did not believe that it was neurofibromatosis, however, because the lesion expanded the bone a bit. I thought that it was a bone cyst. I agree that the three brown spots may have been coincidental. I do know, however, that

you get "my" disease (call it what you will) with lots of brown spots and lots of cysts, with a few brown spots and a few cysts, with no brown spots and one cyst and with one brown spot and no cysts!

DR. CHANNING C. SIMMONS: I cannot reconcile pain with a diagnosis of cyst. As a rule a cyst is painless. Benign tumor is rarely painful and malignant tumor is rarely painless, whereas an inflammatory condition is usually painful. In spite of the normal temperature and white-cell count I do not believe that one can entirely rule out low-grade osteomyelitis that has lain dormant for years.

DR. ALBRIGHT: The pain came on after horse-back riding and presumably was due to a small fracture.

DR. SIMMONS: There is no x-ray evidence of fracture.

DR. ALBRIGHT: There is periosteal proliferation.

DR. SIMMONS: If she had a fracture, I take back that statement. I cannot see any evidence of fracture, however, in these films.

DR. WALTER BAUER: I think if we end up with anything short of a biopsy, we are not going to make the correct diagnosis. I should not be willing to rule out Brodie's abscess as readily as Dr. Daland did, because we know that Brodie's abscess can remain silent for years. We have seen instances where multiple foci of osteomyelitis occurred at the time of the original septicemia, yet only one or two of them became symptomatic shortly thereafter; the other foci gave rise to symptoms one to ten years later. In the last analysis here is a lesion that is expanding and one is certainly not doing the right thing by the patient unless a biopsy is performed and the exact diagnosis established.

CLINICAL DIAGNOSIS

Bone cyst of femur.

DR. DALAND'S DIAGNOSIS

Chondroma of femur.

ANATOMICAL DIAGNOSIS

Fibrous dysplasia of femur.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Dr. Smith-Petersen called me to the operating room just as he was about to unroof the lesion. He removed the cortex over the lesion exposing a cavity completely filled with yellowish-gray, somewhat gritty, fibrous material. A portion of this material was adherent to the

inner aspect of the cortical lid. The cavity was completely evacuated by means of osteotomes and gouges, and the lining was found to be roughened. No fluid or cystic degeneration was present. It was completely solid.

Microscopic examination showed this to be made up of connective tissue with a few small bone trabeculae that were neurotic and poorly calcified. The appearance was quite characteristic of fibrous dysplasia of bone or what Dr. Albright has called "osteitis fibrosa disseminata." We have just recently seen another of these lesions in a rib removed from a twenty-three-year-old girl. This was discovered on routine x-ray examination of the chest before joining the WAVES. Neither of this patient nor the one under discussion had other bone lesions. With the increase in routine x-ray examination we are probably going to see a lot more of this disease and find that it is much commoner than we realized.

DR. ALBRIGHT: Are we talking about the same thing? What do we mean by a bone cyst? The pathological finding was just what I expected.

DR. CASTLEMAN: This is not a bone cyst. It is what has been called by Lichtenstein and Jaffe^{2,3} "fibrous dysplasia of bone," which is apparently a maldevelopment of the mesenchyme as the bone is formed. A solitary bone cyst is quite different. It has a definite capsule and lining and is filled with fluid. Jaffe who has had extensive experience with bone pathology is quite convinced that a solitary bone cyst is an entirely different condition from fibrous dysplasia, although the latter may have areas of cystic degeneration in it.⁴ About half the solitary bone cysts are found in the upper end of the humerus.

DR. ALBRIGHT: I think the terminology is bad all the way through. Let us go back to hyper-

parathyroidism where three things are likely to be present—fibrous tissue, actual cysts filled with fluid, and giant-cell tumors. By x-ray they all look like cysts.

In talking of cysts clinically we do not necessarily mean fluid; it may be fibrous tissue. Perhaps we should. I appreciate that it is loose terminology not to do so, but when all the x-ray interpretations use the same terminology, one gets into bad habits.

I think the bone disease in question had better be called "fibrous dysplasia," as suggested by Jaffe, rather than "osteitis fibrosa disseminata," the term I originally used.

DR. BAUER: I am glad you feel that way about it, Dr. Albright. It will make for less confusion with osteitis fibrosa generalisata—that is, hyperparathyroidism.

DR. CASTLEMAN: The original name that you gave it would be better than "Albright's disease." I think it is unfortunate that we use a man's name to describe these things. We ought to use pathological terms that give visualization of what we see under the microscope.

DR. ALBRIGHT: Yes, but it is rather cumbersome. The term was "osteitis fibrosa disseminata with pathologic pigmentation and precocious puberty in females." I suppose a case with the brown spots and precocity but without bone lesions could be called "fibrous dysplasia sine fibrous dysplasia."

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FE, FI, FO, FUM

THE idea has long been current that if members of the human race—essentially an omnivorous species—wanted good, red blood, they must eat good, red meat. It is a simple, chromatic idea, based on the assumption that like begets like: the closer the color of the meat is to blood, the better the blood it builds. How beef cattle get such good, red blood from the grass they eat is another story; their domestic economy is of a different nature and they are put on earth for man's service.

At any rate, the belief persists that since beef is meat, meat must of necessity be beef. Mutton is

a poor substitute and under suspicion, being not usually of a red color when cooked, and pork, of course, is pork. These are peasant foods and, presumably, not alone capable of preserving the virility of the descendants of the pioneers who first broke the soil of our great democracy.

With war, however, has come the rationing of many things, including food—not entirely for the sake of increasing, with beef, the bellicosity of our armed forces or of overstuffing our British allies, who for four long years have kept alive the flickering flame of freedom. It is mainly that, with limited production, the available supplies should be evenly apportioned and that each should have no less than his share because another wanted more.

To one group of persons special dispensation has been granted, as was their due. This group consists of those afflicted with certain chronic illnesses who would suffer peculiar hardships from accepting the dietary limitations to which the rest of the country has acquiesced. The stewardship of their rations has been placed, logically, in the hands of the medical profession, and already several thousand physician's certificates of patient's necessity have been granted in Massachusetts, the majority of which call for extra meat rations.

It might seem that, among the other great upheavals of the war, the fixed idea that meat must be red could also be uprooted. We are, indeed, reliably informed that lamb, pork, poultry, milk, eggs, cheese and even the lowly fish contain and furnish the same dozen essential amino acids as does good sirloin and that nutritionally these animal protein foods are practically identical—and half of them are not yet on the ration lists. Evidence seems even to be accumulating that man can exist and function on far less than his daily traditional 70 grams of protein. Add to these iconoclastic innovations the eruption of that complete food, the soybean, over the length and breadth of the land, like the dragon's teeth that Cadmus sowed, and roast beef may well go entirely on the luxury list.

CANCER CONTROL

A SYMPOSIUM on cancer control was held in New York City on October 11, the day preceding the opening of the Wartime Conference of the American Public Health Association in that city. Participants included representatives from the National Cancer Institute, the American Society for the Control of Cancer and the American College of Surgeons and from eleven states, two counties and one city having cancer programs, and among the audience were officers of the Women's Field Army.

The symposium was composed of four sessions: the first devoted to epidemiology, the second to administration, the third to service to cancer patients and the fourth to education. Approximately one hundred persons attended all four sessions, and about four hundred attended at least one session.

The symposium indicated that several trends are emerging in cancer control. The desire for prevention, early diagnosis and prompt treatment is manifest throughout the country. More rounded programs consisting of service to patients, research and education are to be preferred to a more limited program.

In New York City a cancer prevention clinic has been in operation for about three years. Approximately 75 per cent of the persons examined were found to have cancer and in most cases the disease was in a very early stage. The extension of the prevention clinic is a strong possibility in future cancer control.

Reporting of cancer, either through the physician or through the hospital, will probably be adopted more extensively in the future. The experience in compulsory cancer reporting by physicians in New York and in the reporting by hospitals in Connecticut indicates that both methods of obtaining a satisfactory knowledge of cancer morbidity are feasible.

A strong trend toward education in cancer in the public schools is being met by various types of programs in many different localities. From

this there may emerge a clear idea of whether cancer education in the schools is expedient, and if so, what its scope should be. The values of different methods of educational approach may well alter future practices. Two experimental school projects in cancer control in Massachusetts were presented at the symposium. In Malden a unit of four lecture periods was conducted in the eighth-grade classes last spring. In Lynn a cancer unit with four elements is being given in the biology classes in one high school and in the public-health classes in another, and the entire school is being instructed through the general assembly in a third. Prior to the inauguration of the Lynn program an estimate of the students' present knowledge of cancer was made by means of a true-false questionnaire. With this as a background, measures of improvement can be made at later periods.

All in all, in spite of the distractions occasioned by the war effort, it is evident that significant advances are continuing in the program devised for the control of cancer.

MEDICAL EPONYM

LAURENCE-MOON-BIEDL SYNDROME

This eponym is applied to a symptom complex described by Solomon Solis-Cohen and Edward Weiss in a paper, "Dystrophia Adiposogenitalis, with Atypical Retinitis Pigmentosa and Mental Deficiency—The Laurence-Biedl Syndrome: A report of four cases in one family," in the *American Journal of Medical Sciences* (169:489-505, 1925), which they thought identical with the conditions described by the authors of the papers here summarized.

In the *Ophthalmic Review* (2:32-41, 1866), John Zachariah Laurence (1830-1874) and Robert C. Moon (1846-1914) published a paper entitled "Four Cases of 'Retinitis Pigmentosa' Occurring in the Same Family and Accompanied by General Imperfections of Development." A portion of the article follows:

Marian T., aet. 7, 3 feet, 8 inches, in height, is a fat, flat-featured, heavy-looking child. . . .

Scattered over the fundus oculi . . . were several irregular figures of a deep black color. . . .

Harry S., aet. 20, is short for his age—measuring only 5 feet, 3¼ inches, in height. He walks with a slouching, heavy gait, as if he were tipsy.

The superficial stratum of the choroid is considerably atrophied. . . . A few isolated dark black pigment spots are scattered over the fundi. . . .

Frederick, aet. 18, measuring 4 feet, 6½ inches, in height, is a fattish heavy-looking boy. . . . Like his brother Harry, he walks with a slouching, helpless gait, dragging his legs from the hips.

Ophthalmoscopic examination showed exactly the same appearance as in Marian's eyes. . . .

Charles, aet. 15, measures 4 feet, 4½ inches. He is dull and inanimate, like the two other youths, and has a slouching gait, but not at all to the same extent as his brothers.

The ophthalmoscopic description of Harry applies to this boy. . . .

The height of each patient has been given for the purpose of directing attention to the dwarfish stature of the boys for their age. The organs of generation are also strikingly implicated in the general want of development.

The arrest of development was by no means confined to the eye, but affected several other organs of the body. In this latter point of view, and more especially when we regard the general imperfection of the mental faculties, these patients may in a certain sense be not inaptly compared to cretins in a mild degree.

In the *Deutsche medizinische Wochenschrift* (48: 1630, 1922), Arthur Biedl discusses this subject at a meeting of the Prague Society of German Physicians. A portion of the translation follows:

A brother and sister with adiposogenital dystrophy and a third patient were characterized by absence of any changes in the hypophysis or of any signs of brain tumor or pathologic intracranial pressure and by the presence of congenital malformations (retinitis pigmentosa, polydactylism and atresia ani), together with limited cerebral development, shown principally by a peculiar mental torpor. In one case a diminished basal metabolism was demonstrable. . . . This new symptom complex is to be attributed to a primary underdevelopment of the brain, especially that part of it containing the metabolism center.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BUEHLER — GEORGE VAN BUSKIRK BUEHLER, M.D., of Bedford, died November 19. He was in his sixty-eighth year.

Dr. Buehler received his degree from the University of Pennsylvania School of Medicine, Philadelphia, in 1895. He was founder of the Cambridge Relief Hospital in 1914. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow and a son survive.

HALLISEY — JOSEPH E. HALLISEY, M.D., of Boston, died November 18. He was in his sixty-second year.

Dr. Hallisey received his degree from Tufts College Medical School in 1908. He was physician-in-chief of the First Medical Service and chief of the Cardiac Clinic at the Boston City Hospital. He was a professor of medicine at Tufts College Medical School and a former president of the Boston City Hospital Alumni Association. He was a member of the Massachusetts Medical Society and the American Medical Association.

LODGE — ATHENS V. LODGE, M.D., of Brewster, died November 18. He was in his seventy-second year.

Dr. Lodge received his degree from the University Medical College of Kansas City in 1900. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a daughter and three brothers survive.

PERCY — KARLTON G. PERCY, M.D., of Brookline, died November 15. He was in his fifty-eighth year.

Dr. Percy received his degree from Harvard Medical School in 1911. He was on the staffs of the Children's Hospital, Boston, Chelsea Hospital, Chelsea, and the Whidden Memorial Hospital, Everett. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son, a daughter, his mother, a sister and a brother survive.

CORRESPONDENCE

THE LATE DR. STETSON

To the Editor: I want to thank you and A.H.E. for the facts that the obituary on Dr. Halbert G. Stetson contained, in the October 28 issue of the *Journal*.

I do not think I ever before realized how cold cold facts can be and, therefore, I should like to add a little more about Dr. Stetson, of whom we were all so fond.

He was a man who, not only when he was president of the Massachusetts Medical Society but before and afterward, gave unselfishly of his time and strength to the Society. As a young man he quite rightly chose to practice in a small county seat and grew up with the community. His endless services to people as well as his medical ability soon gave him prominence. His most outstanding work was with the development of the local hospital. His unfailing kindness and common sense placed him high with all those who were fortunate enough to have been his friends.

The medical profession needs to have more doctors develop in the way Dr. Stetson did.

HILBERT F. DAY

34 Kirkland Street
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ABNORMAL NITROGEN METABOLISM IN PATIENTS WITH THERMAL BURNS*

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THE burned patient is not a simple subject for metabolic study. In addition to the large amount of tissue breakdown and subsequent nutritional demands by the healing processes and the continuous loss of nitrogenous material from the burned surface, the burned patient is seldom free from intercurrent complications. Disturbance of renal or hepatic function may be present.¹ Local and sometimes general infections occur.² Shock may be an early complication and may have protracted secondary effects.³ Fever may be present.² All these complications may cause severe disturbances in metabolism. In spite of these difficulties, a study of the nutritional requirements of the severely burned patient appears to be necessary since the healing of the burned surface may depend, in part, on the maintenance of good nutrition.

This paper presents certain observations on the disturbances of nitrogen metabolism in severely burned patients admitted to the Boston City Hospital as the result of the Coconut Grove disaster. In a subsequent report,⁴ methods for controlling some of these abnormalities in nitrogen metabolism will be presented, and detailed observations on one severely burned patient are given elsewhere.⁵

AZOTEMIA

Azotemia is a known complication of the se-

verely burned patient,⁶ and two distinct types were occasionally observed in the present study

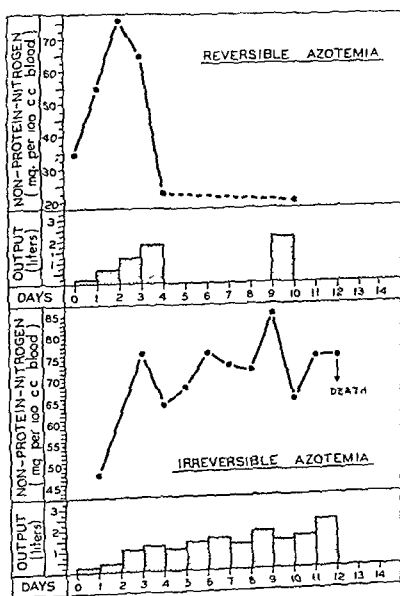


FIGURE 1. Reversible and Irreversible Azotemia, associated with Early Oliguria, in a Severely Burned Patient

A reversible azotemia, associated with transitory oliguria, occurred frequently as an early complication. A typical example of this type of increase in the nonprotein nitrogen of the blood is shown in the upper part of Figure 1. This phenomenon is similar to that frequently found following surgical operations and in shock, when oliguria,

*From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), and the Burn Assignment of the Surgical Services Boston City Hospital and the Department of Medicine, Harvard Medical School.

†The work described in this paper was done in part under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

‡The expenses of this investigation were defrayed in part by gifts from the Josiah Macy, Jr., Foundation of New York, and the Smith-Rime and French Laboratories of Philadelphia to Harvard University.

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or even anuria, may persist for some hours. In this type of azotemia, the restoration of a normal urine output results in a return of the increased nonprotein nitrogen level of the blood to normal. Since, however, the kidney can clear urea only at a fairly fixed maximum rate, the azotemia may persist for several days, as is shown in the patient illustrated in the figure.

Another type of azotemia was found in certain burned patients studied because of the presence of hemoglobinemia and hemoglobinuria. These problems will be discussed elsewhere.⁷ This type of azotemia occurred only in severely burned patients. In these patients from 20 to 55 per cent of the body was burned, and much of the burn was third degree. With one exception, they secreted an acid urine. In a group of 9 patients having these criteria, 6 showed azotemia. In 5 of them the azotemia was irreversible, and in 1 it was reversible.

The nonprotein nitrogen in irreversible azotemia did not rise to the high values usually encountered in renal shutdown and complete anuria. The level was quite constant and seldom rose above 80 to 100 mg. per 100 cc. of blood. A typical example of irreversible azotemia in one of the patients studied is shown in the lower half of Figure 1. It will be noticed that oliguria was present early but that a normal urine output was soon obtained. The urine did not have a fixed specific gravity. In spite of this, the nonprotein nitrogen of the blood did not fall. The patient died on the twelfth day following her injury. It is of some practical importance that sulfadiazine administered to patients with irreversible azotemia gave satisfactory blood levels of the drug and was apparently well cleared by the kidney. Under no circumstances was the drug administered until a normal diuresis was obtained.

It is known that the excretion of hemoglobin in an acid urine may result in deposition of hemoglobin or its derivatives in the kidney.^{7,8} If, however, this was the primary cause of the azotemia, the damage to the kidney was not complete, since, except for an early transitory oliguria, the urine output was normal in volume and total solids. It is therefore suggested that in patients such as have been described an irreversible azotemia can occur owing to a partially damaged kidney. It is also probable that the increased rate of protein catabolism in such severely burned patients was an important additional factor in the production of a high nonprotein nitrogen in the blood. The damage to the kidney alone was not of sufficient severity to account for the nitrogen retention.⁷

NITROGEN PARTITIONS OF BLOOD AND URINE

A partition of the nitrogenous constituents of the blood and urine of 3 patients with severe burns was done. The data of one patient are given in Tables 1 and 2. This patient sustained a

TABLE 1. *Partition of the Nitrogen in the Blood of a Severely Burned Patient.*

DAY	NON- PROTEIN NITROGEN <i>mg./100 cc.</i>	UREA NITRO- GEN <i>mg./100 cc.</i>	CREATI- NINE NITROGEN <i>mg./100 cc.</i>	CREATINE NITRO- GEN <i>mg./100 cc.</i>	AMINO ACID NITROGEN <i>mg./100 cc.</i>	RESIDUAL NITRO- GEN <i>mg./100 cc.</i>
5	75.6	53.2	1.5	0.7	4.4	15.8
6	72.8	53.7	1.6	0.5	4.0	13.1
7	71.1	54.4	1.5	2.0	4.6	8.5
8	85.6	53.2	1.3	2.2	4.6	24.2
9	65.0	45.3	1.0	0.7	4.1	13.8
10	75.0	49.3	1.0	1.8	4.7	18.2
11	74.9	51.1	0.9	1.6	4.6	16.7

thermal burn involving 45 per cent of her body, with 30 per cent third-degree and 15 per cent second-degree burns. She had hemoglobinemia and hemoglobinuria as early complications.

Irreversible azotemia was present, and as shown in Table 1, a portion of the elevated nonprotein nitrogen was accounted for by an increased urea. However, there was present in the blood a relatively large amount of residual or undetermined nitrogen. This residual nitrogen is probably that referred to by Duval et al.⁹ and Lambret et al.¹⁰ as "polypeptide nitrogen." The characterization of this fraction by these authors, however, is far from conclusive.

As shown in Table 2, there was also an increase in the residual nitrogen of the urine. This high level could be equally well accounted for by the excretion of abnormal metabolites or by the presence in the urine of substances that interfered with the action of urease.

Characterization of the residual nitrogen was not attempted. On hydrolysis, it yielded both amino and amido nitrogen. In the present study, the occurrence of a high blood residual nitrogen was not uncommon in severely burned patients, but high urine residual nitrogen was quite rare.

The azotemia illustrated in Table 1 can be accounted for on the basis, previously stated, of the production of large amounts of protein degradation products in the presence of a partially damaged kidney. Liver disease cannot, however, be ruled out in the present series of cases, in spite of the fact that there was no clinical evidence of its presence in the patients studied.

HYPOPROTEINEMIA

The presence of hypoproteinemia in burned patients has previously been commented on.^{2,6} In the present survey, 81 patients with burns were

studied. In 40, hypoproteinemia developed. There appeared to be a definite correlation between the progressive type of hypoproteinemia and the severity of the burn. For example, in 12 patients having burns of between 10 and 50 per cent of the

cases, however, postmortem examination showed some degenerative changes. This subject will be reported on by others.¹¹

It appears necessary to seek causes other than early plasma loss to explain the hypoproteinemia

TABLE 2. *Partition of the Nitrogen in the Urine of a Severely Burned Patient*

DAY	VOLUME cc	TOTAL NITROGEN gm/24 hr	UREA NITROGEN % total	CREATININE NITROGEN % total	CREATINE NITROGEN % total	AMINO ACID NITROGEN % total	AMMONIA NITROGEN % total	URIC ACID NITROGEN % total	PROTEIN NITROGEN % total	RESIDUAL NITROGEN % total
5	1520	8.0	43.5	5.5	0.4	0.9	0.8	1.1	9.6	37.8
6	1600	8.4	20.6	5.2	0.2	1.1	0.4	1.2	1.0	70.2
7	1140	7.0	7.6	4.9	0.0	1.2	0.7	1.3	0.0	84.4
8	1800	12.9	28.7	3.7	1.1	0.9	—	0.9	7.7	57.1
9	1490	11.2	10.0	3.0	0.3	0.9	1.6	0.6	6.3	77.2
10	1580	11.4	13.4	3.3	2.4	0.8	1.7	1.0	1.8	75.7
11	1970	13.9	5.0	7.0	2.7	1.0	2.1	0.6	2.9	82.7

body surface, 8, or 65 per cent, showed progressive hypoproteinemia. In 51 cases with burns involving less than 10 per cent of the body surface, however, only 8, or 15 per cent, showed this abnormal-

of burns. It is a frequent observation that burned patients remaining in a hospital for long periods of time while awaiting skin grafting lose considerable amounts of weight. An opportunity has been given us to study such patients. We found that severely burned patients rapidly lost large amounts of nitrogen into the urine. As shown in Table 3, the nitrogen loss on occasion amounted to as much as 45 gm. a day. It is well known that the excretion of abnormally large amounts of nitrogen occurs in thyrotoxicosis, in severe infections and in other conditions associated with increased metabolism, and it has also been reported as occurring in burned patients.⁶ It has been thought to be due to a rapid destruction of structural protein and has been called by some authors "toxic protein destruction." Obviously, such losses of nitrogen into the urine may cause a marked protein deprivation.

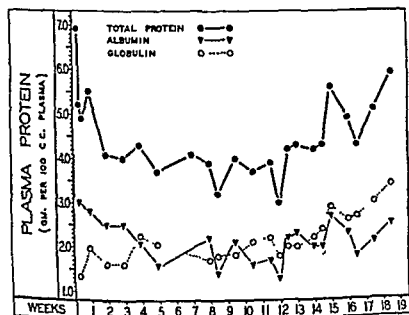


FIGURE 2. *Plasma Protein Fractionation Showing Early and Late Reversal of the Albumin Globulin Ratio*

ity. Early hypoproteinemia was probably associated with protein loss from the burned areas, but other causes must be looked for to explain the progressive type of hypoproteinemia occurring in severely burned patients. This hypoproteinemia increased in severity until the anasarca level was reached and massive edema developed.

The fall in albumin and the reversal of the albumin-globulin ratio encountered early may be theoretically associated with the preferential loss of albumin from the circulating blood owing to the relatively low molecular weight of albumin as compared with that of globulin. It has been noted, as shown in Figure 2, that the albumin level may remain constant while the globulin fraction actually rises in the circulating blood. Such rises in the globulin have frequently been associated with infection and with hepatic dysfunction, as judged by clinical and laboratory evidence. In a few

In all burned patients admitted to this hospital, an attempt was made to meet the demand for protein by increasing the protein intake to from 100 to 125 gm. a day. Even at this level, there was a marked negative nitrogen balance in 9 patients with severe burns. Most of the patients with minor burns of less than 10 per cent of the body surface involved responded to the intake of 125 gm. of protein a day with a return of their plasma protein to normal, but in those patients with a continued marked loss of nitrogen into the urine this did not occur. Indeed, in some of the severely burned patients, it has been calculated that, on the basis of the loss of nitrogen into the urine alone, 300 gm. of protein a day would have been required to maintain nitrogen equilibrium. In addition to this loss, some patients continued to lose large amounts of nitrogenous material from the burned surface for long periods of time. This insensible loss could not be calculated. The restoration of protein under these combined circumstances was a difficult problem, since the amounts required were con-

siderably greater than those the patients could ingest.

A loss of as much as 30 per cent of the body weight has occurred, in some of the patients studied, as a result of failure to maintain adequate nutrition. Therefore, in severely burned patients, a careful appraisal of the nitrogen balance must

Practical considerations of how this problem may be attacked from a nutritional standpoint will be presented in a subsequent communication.⁴

SUMMARY AND CONCLUSIONS

In a series of burned patients, azotemia was a common complication of severe burns and was

TABLE 3. *Excessive Total Nitrogen Excretion, Expressed in Grams per 24 Hours, in Severely Burned Patients.*

Hosp. No.	Day																		
	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	
1088906	6	17	9	32	9	10	7	13	9	10	11	7	4	8	9	10	8	9	
1088895	-	21	22	9	21	25	17	18	19	45	19	13	28	21	38	9	10	13	
1088910	13	16	18	17	-	26	23	14	15	12	11	2	14	15	4	24	21	16	
1088930	10	20	21	-	15	11	25	5	8	14	10	10	11	11	12	11	11	5	
1088865	-	-	22	-	5	13	14	9	11	12	14	8	-	3	16	10	8	15	
1089011	-	11	18	10	15	17	19	22	19	19	28	16	-	14	17	16	14	14	
1088976	-	22	33	9	17	16	29	11	14	13	17	21	8	9	-	4	16	11	
1088892	19	-	34	23	24	30	26	9	30	11	11	24	26	20	19	14	13	20	
1089013	-	17	9	12	17	8	14	18	13	14	18	17	19	20	25	24	22	19	

be made early, and when marked deficits of nitrogen are expected, forced alimentation by a variety of routes should be begun. The problem becomes

usually of the reversible type. It occurred early and was relieved when the urine output became normal. In some severely burned patients, an irreversible type of azotemia occurred. This increase in nonprotein nitrogen was not progressive and may have been due to a partially damaged kidney in the presence of increased protein catabolism. So far this type of azotemia has been chiefly found in severely burned patients excreting an acid urine in whom hemoglobinemia and hemoglobinuria were present.

In certain severely burned patients having coincidentally hemoglobinemia and hemoglobinuria, there was an abnormality in the partition of both the blood and the urine nitrogen, associated with the presence of large amounts of residual or undetermined nitrogen. The percentage of total nitrogen of the urine present as urea was low.

Hypoproteinemia was a common finding in the severely burned patients. A transitory hypoproteinemia was associated with plasma loss and could be restored by simple dietary means, but the more progressive type was probably due to the loss of large amounts of nitrogen into the urine owing to increased protein catabolism, in addition to large losses of nitrogenous material at the burned surface.

Inversion of the albumin and globulin ratio frequently occurred. When it happened early, it was probably associated with a preferential loss of albumin, which has a low molecular weight. The cause of its late occurrence in burned patients has not been determined.

The serious problem of the maintenance of adequate nitrogen metabolism in severely burned patients is briefly outlined.

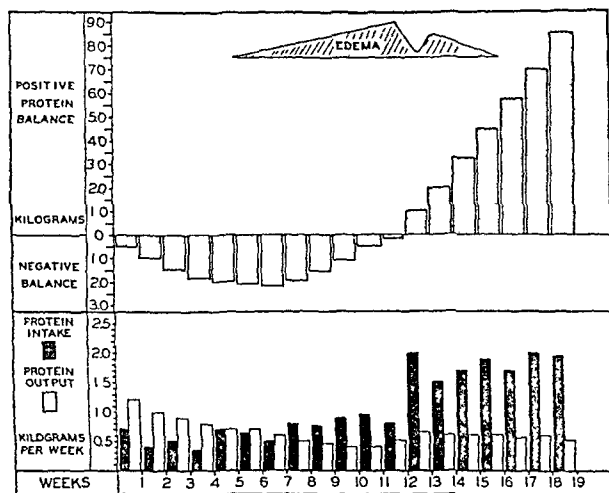


FIGURE 3. *Nitrogen Balance in a Severely Burned Patient.*

increasingly difficult as time goes on, so that whatever measures are to be used to ameliorate the nutritional deficits must be commenced early. It must also be remembered that estimation of the nitrogen requirements of a burned patient by the usual nitrogen-balance studies alone give only the minimum requirement. For example, as shown in Figure 3, in one patient, after positive nitrogen balance was restored by gastric intubation and intravenous amino acid, over 8000 gm. of protein was laid down in a period of six weeks without unusual increases in urine nitrogen and with evidence of complete utilization. Even after this apparently large nitrogen retention was established, the patient was still fifty pounds below the admission weight.⁵

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PREVENTION OF VITAMIN DEFICIENCIES IN WARTIME*

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THE prevention of vitamin deficiencies is an important problem and, if the duration of the war is prolonged, a serious one. Unquestionably nutritional deficiencies already exist in the occupied countries, and the United States will have to play a large part in the feeding of those peoples at a later date. We are shipping an ever increasing amount of food to the United Nations and to our troops abroad.

Our government has instituted a program with which we are all familiar. This includes rationing foodstuffs, increasing production on the farm and in Victory gardens, and preserving food in the home to conserve manpower and material. The Council on Foods and Nutrition of the American Medical Association and the Food and Nutrition Board of the National Research Council function jointly to advise on the rationing of food and the institution of educational programs relative to the food problem.

Vitamin deficiency is but one phase of nutrition. It happens to be the newest one, and the one in which a tremendous amount of work has been done in an incredibly short time. The therapeutic use of vitamins has become routine in all branches of medicine. The altered physiologic states associated with specific vitamin deficiencies are, in general, well recognized and well treated. There are also the milder, less well recognized, multiple deficiencies that are usually the province of the internist or the general practitioner.

The public mind is readily captivated by the concept of vitamins and their alphabetical nomenclature. Health giving properties and the vitamin content of processed foods are emphasized. News paper and radio advertising has aroused public consciousness. Over-the-counter sales of attric

tively colored and packaged vitamin preparations have reached tremendous proportions.

Obviously, the answer to the prevention of deficiencies in the face of increasing food shortage in the future is not more and bigger vitamin pills. This is not so facetious as it might sound, and the physician may have contributed at times to the impression that vitamins by definition are found in pills. To prescribe such preparations without having inquired into the patient's diet and without making obvious corrections is but a gesture in the right direction. There is not sufficient material to supplement the diet of the entire population by concentrates and synthetic material, even if it were economically possible to do so. With rationing and such shortages as already exist, many items that are the richest sources of vitamins are unobtainable in sufficient amounts to be included in the daily diet. It becomes necessary to look a little farther down the list, so to speak, and include larger amounts of less rich but more available foods.

This is well illustrated by ascorbic acid. People have largely depended on a daily intake of orange, pineapple or tomato juice—now obtainable only in limited quantity. The logical answer is the increased consumption of cabbage as salad or of potatoes properly cooked. All fruits, berries and vegetables contain significant amounts of ascorbic acid. In England a Walt Disney like character called 'Johnny Potato' is used in cartoons and posters to popularize the increased consumption of potatoes. Approved methods of cooking are published and prizes offered for novel ways of preparing potatoes without destroying their ascorbic acid content.

Many publications contain tables giving the vitamin values of particular food sources. These are usually unreliable and misleading. They are often based on the fresh uncooked animal or

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vegetable source. The ascorbic acid content of green vegetables and fruits, for example, increases steadily to a maximum just before the fruit is ripe and then decreases steadily. The amount in a given fruit or vegetable is also influenced by proper fertilization and methods of growing. With many fruits an added factor is whether they are tree ripened or picked while green and allowed to ripen in storage. Further, the amount of vitamins contained in food after cooking or preservation varies as the process involves cooking, heating, washing, bleaching or the addition of chemicals. It can be readily appreciated that this multiplicity of factors makes for a wide difference in specimens of food as they are found on the table.

There has been set up a table of figures by the Council on Foods and Nutrition of the American Medical Association giving what constitutes daily vitamin requirements in the light of present-day knowledge. These are admittedly an approximation and at best a rough estimate. Changes must be made relative to age, pregnancy, lactation, infection and specific diseases. Revision of these figures tends to be upward as knowledge concerning the requirements is accumulated. It is well to have some basic table in mind as a point of departure. Special requirements with reference to altered physiologic states and specific diseases will not be discussed, as the present rationing system permits additional food in such cases at the request of the physician.

All known vitamins with the exception of vitamin D are synthesized by plants and used by them essentially for the same purpose as by man and animals. Man, however, is unable to synthesize these compounds, with the exception of vitamin D, and must depend on ingestion for his supply of vitamins or their precursors. Vitamins do not furnish energy and are not building units for the structure of the body, but are necessary for the transformation of energy and the regulation of metabolism. There are many gaps in the details of the physiological chemistry of these substances, but evidence has accumulated so far as the better-known vitamins are concerned regarding the general role that they play in the body. There is also a long list of lesser-known substances that apparently contain vitamins. The knowledge of these is fragmentary, their role in the human body is unknown, and no estimate concerning their requirements can be formed. These will not be discussed, but a review of the better-known vitamins should serve to indicate under present conditions the principal available sources, the changes in diet and certain points of preparation of food in order to prevent avitaminosis.

There is not much danger of avitaminosis so far as the A group of vitamins is concerned, provided that there is an adequate intake of vegetables. The daily requirement for the average person is 5000 international units. This is not increased during body activity, but is greater in lactation and pregnancy. Excluding restricted and scarce items, such as dairy products, eggs and liver, the principal sources are green-leafy and yellow vegetables. A single serving—that is, $3\frac{1}{2}$ to 4 ounces of beet tops, kale, mustard greens, spinach or turnip greens—will supply well over twice the daily requirement. A serving of carrots will supply about the same amount. The same serving of summer squash will provide a little over the daily requirement, and sweet potatoes a little under it.

As another approach to prevention of vitamin deficiency in the A group, the Council on Foods and Nutrition has recommended the fortification of oleomargarine to a level of 9000 international units per pound, so that 1 ounce will provide one fifth the daily allowance. The fortification and wider sale of oleomargarine is barred by law in some states and is opposed by dairymen, but there is no question that it provides a suitable vehicle for vitamin A. There is little difference between butter and oleomargarine except for a lower percentage of unsaturated fatty acids in the latter.

In considering the prevention of deficiencies in the vitamin B group, it should be pointed out that the deficiency of a single factor is an exception rather than the rule. These vitamins resemble enzymes and are concerned with the utilization of specific food substances. For example, the riboflavin enzyme system is concerned with the utilization of the essential amino acids, and a deficiency of such amino acids would eventually produce the clinical picture of riboflavin deficiency.

The known members of this group consist of thiamine, riboflavin and niacin. The other members have not been identified or have been studied so inadequately that their function and requirements are unknown.

Thiamine is said to be required in a daily dose of 1.8 mg. for the average person. This requirement is increased with activity, and also during pregnancy and lactation. The outstanding source of thiamine is lean pork. One 4-ounce serving provides almost the daily requirement. The next richest source is dried brewer's yeast, an ounce of which is equal to about the same amount. Thiamine is usually obtained in small quantities from a great many foods, including meat and vegetables. The most available sources are whole-wheat bread and whole-grain cereals. Dried peas and beans are also important. The problem of thia-

mine deficiency is obviously more acute now, with the rationing of meat and a probable decrease in the supply of pork as the war continues. Furthermore, the available amount of brewer's yeast, which is the principal source of natural thiamine concentrates used therapeutically, is inadequate.

This problem was a real one in England and was solved satisfactorily by the increased consumption of peas, beans and other sprouts. The bread in current use for the last several years in England has been made from an 85 per cent extraction flour. Sydenstricker,* who recently described his experience in examining several thousand persons in all parts of the British Isles, stated that the incidence of vitamin B group deficiencies is extremely low. He added that many people were homeless and so closely touched by the war that their incentive to consume these rather unpalatable foods as a constant diet is greater than before.

It is of interest in this connection that one of the largest baking companies in the United States bought the Earle flotation process—a method of getting rid of the woody portion of the hull, which lends a bitter taste to cereal products. This company developed the process, adapted mills to its use, and attempted to market an almost 100 per cent whole-grain bread that was priced the same as the usual white loaf. In spite of a vigorous advertising campaign, the bread did not sell, although it was recommended by nutrition authorities. The experiment was given up except in a few communities that are used as a barometer for public buying tastes.

From a scientific standpoint it would seem that to extract and bleach flour, reducing the vitamin content to about 10 per cent of the whole grain and then fortify it with vitamin concentrates, is a wasteful procedure. On the other hand, if the public will not eat whole-grain bread, this may be the only way that a deficiency can be prevented. Bread also provides a useful vehicle for the addition of riboflavin to the diet.

The next most important factor in the vitamin B group is riboflavin. The requirement is approximately 2.7 mg. per day, or almost twice that of thiamine. The requirement is increased with activity, is in proportion to body weight, and is higher in lactation and pregnancy. Milk is the most important source; one pint supplies half the daily allowance. Meat is another important source, the usual serving supplying about one twelfth the daily allowance. The richest source is liver—4 ounces yields over 3 mg. Riboflavin is readily destroyed by light; it is soluble in water and therefore there are losses in cooking. Omitting

liver and brewer's yeast, which cannot be advocated for general use because of their limited supply, one comes again to the dried sprouts and vegetables such as peas, beans, spinach, cauliflower and peanuts. An increased consumption of these items, together with a pint of milk daily and the use of enriched bread, is the principal method of combating riboflavin deficiency. It should be emphasized that evaporated, powdered or skim milk can be substituted for fresh milk. It is important too that milk that stands in clear glass bottles in sunlight soon loses its riboflavin content.

Niacin, formerly called nicotinic acid, is the third important member of the vitamin B group. The daily allowance is ten times that of thiamine, or 18 mg. The outstanding source is liver, a 4-ounce portion containing somewhat more than the daily requirement. A serving of red meat will furnish from 7 to 10 mg. in each 4 ounces. Dried brewer's yeast in the amount of 1 ounce yields well over half the daily requirement. This vitamin is relatively stable to heat and there is little loss through cooking, although it is soluble in water. Here again, bran and whole-grain cereals are the most important available sources, although peanuts, potatoes and carrots must be included.

The members of the vitamin B group are often discussed together. Their high value in liver, brewer's yeast and meat, all of which are limited in supply, added to the fact that their best secondary source is whole-grain cereals and legumes, indicates a number of points in common. As already stated, there is reason to believe that the general public does not react favorably to dark whole-grain breads and cereals. Bakers are now launched on a program of enriching bread with these three factors. This may be the answer to the problem, although as the war continues it may prove necessary to return to peas, beans, dark bread and potatoes in far greater quantities than anyone would enjoy. The physician in his daily contact can do a great deal to encourage the use of these items. In order to increase the consumption of such carbohydrates fat is necessary: first, because carbohydrate is eaten more easily if it is greased with butter, margarine or drippings; and second, because fat acts as a thiamine sparer in the body.

It is of interest that tests have been conducted on bread to show the loss of vitamin in baking. The bottom crust may show a loss up to 34 per cent of the total thiamine, whereas the top crust may show a loss up to 13 per cent. Toasting a slice of bread destroys somewhere between 11 and 25 per cent of the total thiamine content, depending on the time of toasting and the thickness of the slice.

*Sydenstricker, V. P. An address given at the Medical College of Virginia, March, 1943.

A consideration of vitamin C shows little reason why there should be any extensive deficiency. Although transportation and preserving facilities limit the supply of the favorite sources, such as oranges, tomatoes and pineapple juice, an adequate intake of a variety of home-grown and preserved berries, fruits and vegetables will ensure sufficient vitamin C. Raw cabbage and potatoes are good sources. The average adult requires about 75 mg. The vitamin may be lost in cooking, both because it is soluble in water and because it is destroyed by oxidation.

Previous reference was made to the method of preparing potatoes. A 5-ounce serving of boiled or baked potato provides 25 mg. or about one third, the daily requirement. When potatoes are fried, the ascorbic acid is cut in half. Mashed potatoes show a severe reduction in the vitamin C content, and whipped potatoes lose the entire amount.

Vitamin C has been shown to be present in sweat, as is thiamine. It is known that riboflavin is needed in proportion to body activity. It has been suggested that in addition to feeding salt tablets to defense workers in heavy industry or under conditions of increased heat, thiamine, riboflavin and ascorbic acid be added either in the form of concentrates or as further allowance of food.

The average adult has little possibility of developing a vitamin D deficiency except in conditions of unusually scant exposure to sunlight. This vitamin is synthesized by the body and there is excellent storage. In the winter months an adequate intake should be assured through the diet or by the routine ingestion of concentrates. The outstanding source is fish-liver oil. Some varieties contain as much as 40,000 international units per gram of extracted material. Others contain little or no vitamin D. Eggs are an excellent source, and liver is of definite value. The acuteness of the problem varies with the available supply of these items.

It has been demonstrated that irradiation gives cereals, meat, milk, eggs and various oils antirachitic properties. At the present time milk is the most suitable medium for irradiation and is available in most urban communities.

A point that is insufficiently emphasized with reference to the fat-soluble vitamins A and D is the ingestion of mineral oil. This substance is inert and is not absorbed. It has been conclusively shown that absorption of the fat-soluble vitamins does not take place to any extent from a mineral oil solution. There are many patients who use large amounts of mineral oil over long periods of time. The use of mineral oil salad dressing in reduction diets means the constant ingestion of mineral oil with the food and is of questionable advisability. If used, mineral oil is best taken at bedtime after digestion of the evening meal is completed, when it interferes as little as possible with the absorption of vitamins A and D.

CONCLUSIONS

Deficiency in the A group of vitamins can be avoided by the daily intake of green-leafy and yellow vegetables, and by the use of fortified oleo-margarine when dairy products are unavailable in adequate amount.

Deficiency in the vitamin B group is best controlled by the use of fortified bread, and the physician should encourage the use of whole-grain bread and cereals. The constant use of toasted bread should be discouraged. The average adult should drink a pint of milk a day, or its equivalent in the form of evaporated or dried milk used in food.

Ascorbic acid deficiency can be prevented by the increased use of a varied diet containing fruits, berries and vegetables.

Deficiency in the vitamin D group can best be prevented by adequate exposure to sunlight and the ingestion of eggs and liver when available. If these foods are unavailable, irradiation of food may become more widespread. The routine use of fish-oil concentrates may be advisable under special conditions.

The physician should assume greater responsibility in advising patients with regard to diet. The war may serve the purpose of improving food habits and introduce improved methods of cooking and preserving food.

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ERYTHROBLASTOSIS FETALIS OF THE ICTERUS GRAVIS TYPE

Report of Two Cases With Recovery

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RECENTLY 2 babies showing erythroblastosis fetalis of the icterus gravis type were delivered at the Salem Hospital, and both recovered following a course of treatment instituted in accordance with the recently devised ideas concerning the etiology of this disease. These results seem of sufficient interest to warrant presentation of the cases.

The concept that the production of erythroblastosis fetalis is the result of isoimmunization of the mother to the Rh factor of the fetal erythrocyte, as first shown by Levine, Katzin and Burnham¹ following the demonstration of the existence of the Rh agglutininogen by Landsteiner and Wiener,² is now generally accepted, and both these cases fit into this already familiar pattern (Table 1). In accordance with this theory, therefore, the

TABLE 1 Presence of Rh Agglutinogens in the Families Studied.

CASE NO	FATHER	MOTHER	SIBLING 1	SIBLING 2	SIBLING 3
1	+	—	+	—	—
2	+	—	+	+	+

*Cases under discussion

treatment of the newborn infant manifesting any one of the three clinical types of this syndrome should be directed toward maintaining a satisfactory level of hemoglobin and red cells within the circulation by the administration of Rh- blood of the proper group, so that the patient may be carried over the first crucial days by transfused blood until the anti-Rh substance within the circulation has been eliminated, the destruction of red cells by this phenomenon ended, and the immature cells allowed to mature normally and to assume the function of oxygen transport.

The mortality of erythroblastosis of the icterus gravis type has been generally accepted as relatively high, two publications giving the percentage as 80³ and 75 per cent.⁴ The recovery in the cases here presented, although perhaps not statistically significant, seems to be important and in accord with the changed concept of the fundamental physiology and indications for treatment of this disease. In retrospect, the results indicate that the

previously accepted therapy in such cases, which usually consisted of administering blood taken from the father or some member of the family of the same blood group as the infant and compatible by the usual technic of cross-matching set up at room temperature, has oftener than not been deleterious. The probability is that these donors were of the Rh+ type and that administration of their blood to the infant added insult to injury by supplying the blood stream with more cells to be agglutinated by the anti-Rh substance in the circulation.

It seems worth while to point out, although it has been previously stressed in a recent paper and editorial in the *Journal*,^{5, 6} that determination of the presence or absence of Rh agglutinogens in the blood of the donor should be done before transfusion of the infant showing evidence of erythroblastosis, or of the mother if indicated, and that this procedure ordinarily takes two hours according to the original technic of Landsteiner and Wiener.² With the use of human anti Rh serum the test can be read in a shorter period of time, usually within an hour.

Although we agree entirely with the suggestion that Rh typing should be routine before all transfusions, it also seems important that it be commonly understood that the agglutinin operating in this phenomenon has a very narrow range of temperature specificity, operating at body temperature (37.5°C.) but not at ordinary room temperature. This lack of knowledge of the zone of temperature specificity provides an explanation of why seemingly properly grouped transfusions between the father or other persons and the infant, before the knowledge of the Rh factor was available, proved to be harmful. Therefore, it seems reasonable that anyone showing evidences of the result of isoimmunization to the Rh factor, whether it be the infant or the mother, and—equally important—any Rh- patient receiving multiple blood transfusions, should be safeguarded by setting up the crossmatching at a temperature of 37.5° C. for at least thirty minutes, or longer if possible. In small hospitals where Rh determinations with known anti Rh serums are not routine because of several factors—including an insufficient number of typings to keep changing personnel familiar with the interpretation of the test,

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which is a difficult procedure, the expense and the fairly rapid deterioration of the typing serum—crossmatching at 37.5°C. is easily carried out, and its interpretation by inexperienced persons is simple. It not only detects Rh incompatibility, and must be done to supplement Rh typing, but

suggesting Rh isoimmunization. Both parents were healthy, with no history of tuberculosis, diabetes or blood dyscrasias. The health of the mother during this pregnancy was uneventful. The patient, an 8-pound, 15-ounce girl, was delivered normally after a 12-hour labor with Nembutal and scopamine medication, supplemented during the second

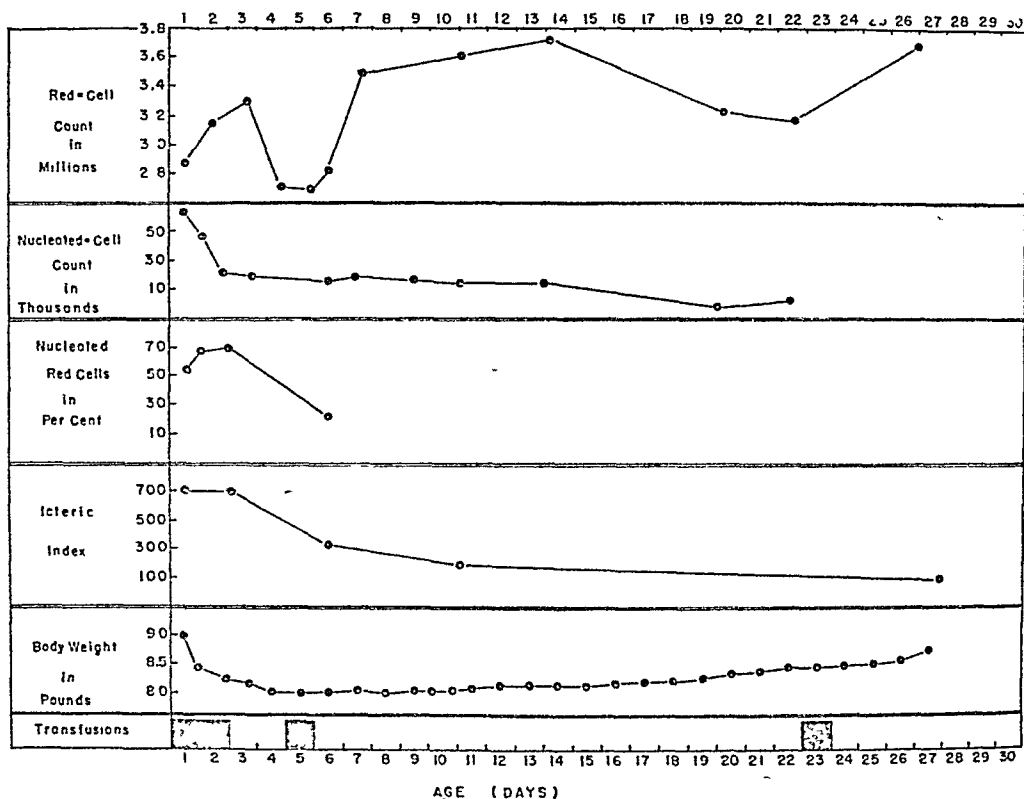


FIGURE 1. Case 1.

may also demonstrate agglutination due to blood subgroup incompatibilities, and furthermore can be done quickly in emergencies.

Another departure from the routine care in these 2 cases was to forbid nursing by the mother. This was done on the assumption that the anti-Rh substance might be transmitted through the breast milk, a possibility suggested by a recent case report.⁷ Since both these children were critically ill, it was thought unwise to jeopardize them further by allowing them to nurse.

A problem that is unanswerable at the present time but is highly pertinent is whether in this type of erythroblastosis permanent damage to the brain may result from the severe degree of kernicterus. This was probably present in each of these cases, since the icteric index at its peak was estimated at 600 and 700, respectively. All that can be said is that after four months there is no clinical evidence of damage to the central nervous system in either case.

CASE 1. F. I. H. This patient was the result of a second pregnancy, the first having resulted in a miscarriage

stage with nitrous oxide, oxygen and ether. Considerable meconium was passed during the delivery, and at birth the patient was covered with bright-yellow vernix caseosa. Because of this, and because the placenta was large and edematous, a specimen of the cord blood was sent to the laboratory to be examined for the Rh factor and was subsequently reported as positive. No anti-Rh substance could be demonstrated in the maternal blood 5 days after delivery.

Twelve hours after delivery, because of respiratory distress, a pediatric consultation was obtained. Physical examination at that time showed deep, golden-yellow jaundice of the skin and scleras, in addition to marked pallor and respiratory distress. The latter was thought to be due in part to the existing anemia as well as to a distended abdomen, caused mostly by a greatly enlarged liver that reached nearly to the iliac crest and by an enlarged spleen that was felt 3 fingerbreadths below the left costal margin. The kidneys were not palpable. The heart was not enlarged and its action was good, with no murmurs. The blood-cell count showed 2,880,000 erythrocytes, 58,000 nucleated cells, of which 51 per cent were red cells, and a hemoglobin of 12.6 gm. (Fig. 1).

Because of pallor and respiratory distress the patient was placed in an oxygen tent. A transfusion of 60 cc. of citrated Rh- blood was given at 12 hours of age, and was repeated at 36 hours because extensive edema of the skin, eyes, scalp, chest, legs and arms had developed

Following the second transfusion, the patient was removed from the oxygen tent, since the generalized edema had begun to subside, and the respirations and color had improved. The icteric index remained at 703. Urinalysis revealed a positive test for bile, a slight trace of albumin and some white and red cells in the sediment.

There was no vomiting of the formula. The nutrition was good. The reflexes were not hyperactive, and development seemed to be progressing normally.

At thirteen months of age, this child had six erupted deciduous teeth, all of which had a deep greenish appearance, presumably due to discoloration by bile pigment.

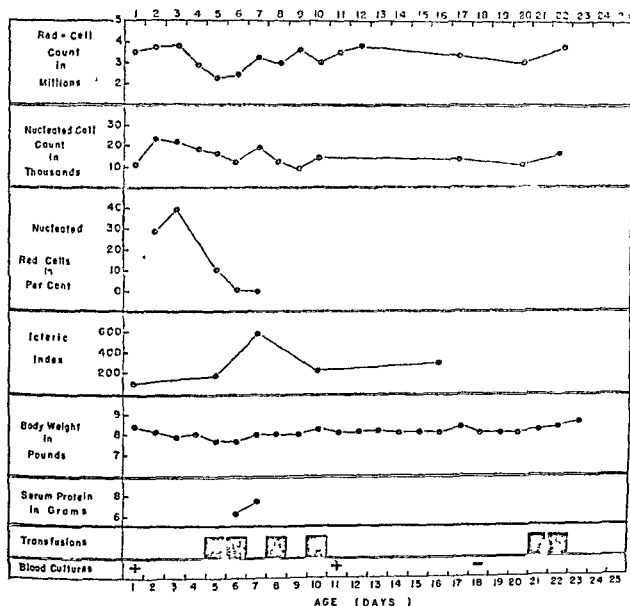


FIGURE 2. Case 2.

The nonprotein nitrogen was 91 mg. and 44 mg. per 100 cc. on successive examinations during convalescence. There was no albumin, bile or cells in the urine at discharge. The serum protein fell to 5.15 gm. per 100 cc. on the 5th day, and because the hemoglobin had dropped to its lowest value (11.6 gm.) and the red-cell count was 2,600,000, a third transfusion of 60 cc. of Rh- blood was given. The blood for all three transfusions was from the same donor. Just before discharge a fourth transfusion was given, using the same donor. The stools revealed negative guaiac tests and negative cultures for pathogenic organisms, and bile tests, at first positive, were negative at the time of discharge. A blood culture taken on the 4th day of life was reported positive for *Staphylococcus aureus*, with slight hemolysis. A repeat culture was not obtained because the external jugular veins were thrombosed, and on account of the later course, the organism was thought to have been a contaminant. A Hinton test on the cord blood was negative. The patient was not allowed to nurse and took well, with little vomiting, a modification of milk, water and Karo.

At discharge the skin still had a moderately jaundiced hue, but on subsequent check-up examination this had completely disappeared and the patient seemed well.

this serves as confirmatory evidence of the marked jaundice at birth.

CASE 2. M. I. M. This patient was the third baby in the family, the two other siblings being a healthy boy and girl aged six and three years, respectively. There was no history of familial disease, including blood dyscrasias. The mother had no complications during this pregnancy and after a short labor was delivered normally of an 8½-pound boy.

At delivery several purplish spots were scattered on the baby's skin. The temperature was 96°F. rectally. He was jaundiced. Vitamin K was given intramuscularly and a pediatric consultation was obtained.

Physical examination at that time revealed several scattered purplish, ecchymotic areas in the skin of the face, extremities and trunk, moderate icterus of the skin and scleras and moderate pallor of the lips and mucous membranes. The liver was palpable two fingerbreadths below the right costal margin, and the spleen was felt one fingerbreadth below the left costal margin. Examination of the blood showed a bleeding time of less than 2 minutes, an erythrocyte count of 3,900,000 and a total nucleated-cell count of 13,500, of which 31 per cent were red cells, and a hemoglobin of 16.5 gm. (Fig. 2). The icteric index

was 160. The direct blood bilirubin was 5.3 mg. per 100 cc., and the indirect 0.69 mg. There was no bleeding from the mouth or cord. Urinalysis showed no red cells, and a guaiac test on the meconium stools was negative. A blood culture was taken and was reported positive for *Staph. albus*, but a repeat blood culture made a day later was reported as negative. The maternal blood was Rh-, and the undiluted serum taken 3 days after delivery showed agglutination of one of three known Rh+, compatible bloods. Blood determinations were made daily, and on the 2nd day the nucleated-cell count rose to 26,000, with 41 per cent red cells. No more ecchymotic spots appeared on the skin, and those present gradually faded and disappeared (Fig. 2). The icteric index on the 5th day was 200. The nonprotein nitrogen was 50 mg. per 100 cc. The hemoglobin had fallen to 12 gm. and the red-cell count to 2,670,000. The urine contained large amounts of bile and the stools were deep green, presumably owing to biliverdin, with persistence of this coloration until the 10th day. Since on the 5th day respiratory embarrassment had set in, the patient was placed in an oxygen tent. Because the pallor had become more marked and the liver and spleen had increased in size, he was transfused with Rh- blood.

For the next 2 weeks the illness was severe, despite a second transfusion with Rh- blood on the 6th day. The donor was the mother of the patient in Case 1, her baby at that time being 2 months old. The icteric index increased to 600 and the hemoglobin fell to 10.5 gm. A third and a fourth transfusion with Rh- blood were given on the 8th and 10th days, and although the hemoglobin did not rise significantly and the icteric index remained at 600, the color improved. No edema of the tissues developed, and the serum protein value of the blood remained normal. The patient was removed from the oxygen tent since the respirations were no longer labored. There continued to be large amounts of bile in the urine, and the sediment showed granular casts and occasional white and red cells. The stools also contained large amounts of bile but were negative for blood, and cultures were negative for pathogenic organisms. By the 18th day the icteric index had fallen to 300 and there was improvement except for the pallor. On the 21st day, the hemoglobin was 11.2 gm., the red-cell count was 3,200,000, and because the white-cell count was rising and another blood culture was reported positive for *Staph. albus*,—a subsequent blood culture was reported negative,—a fifth transfusion was given, the blood from the original donor being used. Following this the baby again became more jaundiced. Efforts to obtain blood for a repeat icteric index were unsuccessful. The hemoglobin and erythrocyte count, which were 13.9 gm. and 4,190,000 following this transfusion, slowly dropped, but with a sixth and last transfusion the blood remained at a satisfactory level, the jaundice slowly disappeared, and the patient seemed well. During his entire stay in the hospital he was not allowed to nurse and was placed on a modification of cow's milk, water and Karo, digesting this well without vomiting.

Subsequent check-ups have shown that so far the reflexes are not hyperactive; the patient's development seems to be within normal limits, and his nutritional status is good.

At the age of eleven months this child had eight deciduous teeth, all of which had the same deep greenish discoloration as those seen in Case 1.

DISCUSSION

It seems certain that the important life-saving factor in the treatment of these infants was the use of Rh- blood of the proper group in the early days of life. This, then, places a serious responsibility on any hospital to maintain either a current supply of Rh- blood of the various groups or a file of Rh- donors. In this connection, it might be worth while to consider some plan whereby hospitals strategically located and having blood banks, possibly those that are subsidized by the federal government under the Office of Civilian Defense, would be utilized as depots for Rh- blood. The expense of doing Rh typing on all donors might be defrayed by some state agency interested in maternal and infant welfare, and these depots would be subject to call from any hospital in the vicinity to provide the proper type of blood.

In the second case presented, it is noteworthy that the other two siblings, who showed no evidence of erythroblastosis at birth or subsequently, were both Rh+, and one may speculate that at the time of those births the development of the anti-Rh substance in the mother did not reach a sufficiently high level to damage seriously the cells within the fetal circulation. It may also be true that owing to the previous immunization to the Rh factor, the mechanism was accelerated during the third pregnancy.

From our one and a half years of experience with the Rh factor as related to isoimmunization in pregnancy, we have been led to develop a routine on all prenatal patients according to which the Rh factor and blood group are determined early in the course of the pregnancy, preferably when blood is taken for the Hinton test. If the mother is Rh-, or if there is history of erythroblastosis, stillbirths or miscarriage that suggests that isoimmunization of pregnancy may have occurred, blood is taken from the husband and siblings for determination of the Rh factor and blood group. If the mother is Rh- and the father Rh+, routine determinations of the former's serum are done biweekly from the seventh month on to determine whether any demonstrable anti-Rh substance can be found. This is performed by mixing the unconcentrated serum with a 2 per cent suspension of ten Rh+ bloods of the same blood group. If the patient's serum agglutinates a majority of these bloods when incubated at 37.5°C., the finding is taken as significant, and if possible, a titer is determined on a dilution basis. Demonstration of a significant and a rising titer is sufficient evidence to warrant prompt delivery of the infant—provided the baby is viable—to prevent excessive flooding of the

fetal blood stream with anti-Rh substance and possible intrauterine or neonatal fetal death

The determination of the blood group serves two purposes. First, it is a matter of convenience to have the group known in the laboratory in the event that transfusions are needed in the treatment of any of the complications arising from the pregnancy. Second, since occasional cases of isoimmunization to factors other than Rh, such as the blood subgroups, have occurred and have been estimated to be responsible for 2 per cent of the cases of erythroblastosis fetalis, the determination of the blood group is important.

Demonstration of the anti Rh substance in the breast milk⁷ and the clinical impression gained by us that infants showing no evidence of erythroblastosis but whose mothers showed an anti-Rh factor in their blood stream did not do so well as expected have led us to the decision not to allow them to be breast fed until further experience has been gained in the study of a large series of cases.

SUMMARY

Two cases of erythroblastosis fetalis of the icterus gravis type resulting from isoimmunization to the Rh factor, with apparent complete recovery, have been presented. Salient facts relative to the immediate care of the baby, with emphasis on the understanding of the mechanism of isoimmunization, have been discussed.

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CLINICAL NOTE

OTOGENOUS INFECTION DUE TO THE PROTEUS BACILLUS

REPORT OF A CASE

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THE emphasis on the rarity and severity of otogenic infections by the proteus bacillus (*Proteus vulgaris*), expressed in a recent paper by Gerzog,¹ makes it worth while to report an additional case. According to Gerzog, previous to the case that he reports with recovery, only 9 cases had been reported in the literature since 1912. Only 1 patient survived, and this was the only case in which there was not a positive blood culture for this organism. Three patients, he states, died of meningitis and 5 of overwhelming bacteremia. The case to be reported is unique because the patient survived after having had a positive blood culture.

CASE REPORT

C K., a private patient of Dr Warren W Marston, was a 25-year-old man who had had a right chronic suppurative otitis media, with a foul odor, for most of his life but had otherwise been well. The previous year

he had had a tonsillectomy, which did not change the ear condition.

On April 2, 1940, the patient began to have headache on the right side. This persisted until April 7, when he vomited all day and had a chill at night. He was sent to the Newton Hospital. On admission the temperature was 100.2°F rising that evening to 102.8°, and the white cell count was 13,600 with 92 per cent neutrophils. At the first operation, performed by Dr Donald H MacDonald on April 9, the mastoid was opened and was found solidified with ivory-like sclerosis, a culture yielded an identified gram negative bacilli and *P. vulgaris*. The lateral sinus at that time was not uncovered and the jugular vein was not ligated. For 3 days the patient was given large doses of sulfapyridine, and this treatment was followed by a temporary subsidence of the temperature.

On April 14, the temperature rose to 103.3°F and the pulse to 120, a blood culture was reported negative. On the following morning the patient had a chill and that afternoon the temperature rose to 103.1°F, the white-cell count being 10,700. At that time I saw the patient in consultation. Sinus phlebitis was believed to be the diagnosis, and further operation was advised. A lumbar puncture was performed on the same day, and the dynamics disclosed that the right jugular vein was blocked. On April 16 the jugular vein was ligated, the mastoid reopened and the sigmoid sinus uncovered. The mastoid antrum was reamed larger, and the dura uncovered. A liquid foul smelling pus kept accumulating in the antrum. Following incision of the membranous wall of the sigmoid sinus, there was an escape of foul pus. A culture from this showed *P. vulgaris*, and the same foul odor was present in the culture tube. Since it was believed that the abscess was walled off within the sigmoid sinus, no further exploration was attempted. The mastoid cavity was filled with iodoform gauze, and the mastoid wound was approximated to the drain. The patient again was put on large doses of sulfapyridine.

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For the next few days, the patient ran a spiking temperature, which rose as high as 104.8°F. On April 18, the white-cell count was 45,500, with 93 per cent neutrophils. Because of continued fever, with occasional chills, and three successive blood cultures that were positive for *P. vulgaris*, it was believed that the infection must be coming from the torcular end of the right lateral sinus. Hence, on April 22 the patient was again operated on, the lateral sinus being uncovered all the way around to the torcular by removing the overlying bone of the skull. The lateral sinus itself was then opened and found filled with grayish pus all the way around to the vicinity of the torcular. Owing to the danger of pushing the last walling-off into the venous circulation on the left side, further exploration was terminated and iodoform strips were laid in the opened lateral sinus. The incision was approximated with interrupted silk sutures. Following this operation there were no more chills, and within a few days the temperature and white-cell count were normal. Subsequent blood cultures were negative, and the patient made a slow and uninterrupted convalescence.

A year later a successful radical mastoid operation aided by skin grafting was performed, which eliminated discharge and odor.

Since Gerzog's paper was published, 2 more deaths have been reported. These additional fatal cases emphasize the grave pathogenicity of the proteus organism. Even the new chemotherapeutic drugs seem to have failed to stem its serious ravages.

In 1940, Neter and Chait,² of Buffalo, reported the case of a fourteen-year-old girl who was oper-

ated on for chronic mastoiditis due to an infection with *P. vulgaris*. This case was complicated—by meningitis as well as by septicemia. In spite of surgery and chemotherapy the patient died on the eighth day. In 1943, Adler and Klapper,³ of New Orleans, reported the case of a twenty-eight-year-old man with proteus infection of the mastoid. The symptoms were high fever, chills and vomiting. There was a positive blood culture for *P. vulgaris*, but no meningitis. Despite the use of sulfathiazole, sulfadiazine and finally sulfapyridine, the patient died on the twenty-second post-operative day. Autopsy revealed thrombosis of the lateral sinus, extradural abscess and a pulmonary abscess in each lung.

SUMMARY

A successfully treated case of otogenic infection due to *Proteus vulgaris* and complicated by septicemia is reported. The pertinent recent literature is reviewed.

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MEDICAL PROGRESS

THE TREATMENT OF THERMAL BURNS*

II. Recent Developments

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THIS review is intended to summarize recent developments, and supplements the general outline prepared by the National Research Council.¹ The important articles of 1943 on the fundamental concepts of burns that should be read by every physician are those by Whipple,² Trueta,³ Glenn, Gilbert and Drinker,⁴ Barnes and Trueta⁵ and, in spite of the fact that it concerns wounds rather than burns, that by Orr.⁶ The best short

description of the most significant phases of local and general treatment of burns may be found in Volume V of *Military Surgical Manuals*.⁷ Harkins's⁸ book may be consulted for a complete résumé of the history of burns.

DETERMINATION OF DEGREE OF INVOLVEMENT OF THERMAL BURNS

The determination of the depth of a burn is of the greatest importance, because in the past many authors have claimed that by using a given treatment a burn was maintained as a burn with destruction of only part of the epithelial cells (second degree), whereas if any other treatment had been used the burn would have been one destroying all the epithelial cells (third degree). Usually

*The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C. Thomas, 1942. \$5.00).

†From the Burn Assignment of the Surgical Services of the Boston City Hospital and the Department of Surgery, Harvard Medical School.

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such claims were made without any detailed description of the differentiation of the various types of burns.

A fresh burn with erythema, a moist surface, multiple broken or unbroken blisters, moderate edema of the skin and no subcutaneous edema is probably a part-thickness burn. A fresh burn with a dry, leathery, dead white or brownish appearance is probably a full-thickness burn. But there are areas in many cases where no clear cut diagnosis can be made early.⁸⁻¹⁰ *The time when classification of the depth of burns should be made is after healing has occurred or successful grafting has been done.*¹⁰ The recognition of this fact is important because the elimination of unwarranted claims, based on impossible distinctions, from serious consideration is definitely a step toward scientific thinking.

TREATMENT OF MINOR BURNS

In small-area burns systemic effects such as shock can usually be disregarded. The important considerations in these cases are rapid healing, prevention of infection, minimizing of pain and reduction of disability during and after treatment.

Rate of Healing

Cannon and Cope¹¹ and Hirshfeld, Pilling and Maun¹² have shown that skin-graft donor sites, which are somewhat but not perfectly analogous to burns, heal much more slowly if escharotics such as tannic acid or triple dye are used than if boric acid ointment is employed. Taylor¹³ has demonstrated the same thing with second-degree burns. Clowes and his associates¹⁰ have shown that tannic acid-silver nitrate treatment delays the healing of burns. Their evidence in regard to triple dye is not so clear cut, but points in the same direction. They also found that there is a regional difference in the time of healing of burns treated by any given method, with the face healing more rapidly and the back more slowly after part-thickness burns than any other areas of the body.

Prevention of Infection

In spite of all the claims that have been made, there is no known method of keeping any burn sterile. A part-thickness burn will harbor pathogenic organisms in most cases, even when the treatment is carried out by groups specially equipped for the study of these cases.¹⁴ Cope¹⁵ has recently shown, however, that if a burn is dressed with a simple ointment without cleaning it, but with a bulky pressure dressing *that is left alone*, and the patient is given sulfadiazine systemically, the infection is relatively harmless. Infection has been found under the plaster casts of Levenson

and Lund¹⁶ and of Logie,¹⁷ but serious infection in minor cases has not been reported with this treatment. Sulfanilamide and related compounds applied locally have given good results in many cases,¹⁸ but their application in powder form may result in dangerously high levels in the blood.¹⁷ Their local use has been bacteriologically disappointing.¹¹⁻¹⁷ Intercurrent infection of burns at the time of dressings may be a much more serious matter than has until recently been recognized.¹⁰ In addition to careful aseptic technique at the time of dressing, Allen and Koch,²⁰ Siler and Reid,²¹ Owens,²² Cope,¹⁵ Gurd, et al.,⁹ Clowes,¹⁰ Trueta,³ McClure²³ and Levenson¹⁶ all stress the value of infrequent dressings as another factor in reducing the danger of infection, even though there are minor differences in their methods. Clark and his associates¹⁹ have studied the use of penicillin and of propamidine as agents to control streptococcal and staphylococcal infections, with promising bacteriologic results. Their method, however, entailed two dressings a day, and their cases healed no more rapidly than have similar cases treated by more widely available methods. On the other hand, as penicillin becomes available in larger quantities and can be used in larger doses, it may become an extremely valuable therapeutic agent.

Prevention of Pain

The greatest cause of pain in burns is caused by friction under a dressing or by the changing of dressings. A second-degree burn should be and can be kept painless by a properly applied pressure dressing or cast from the time of first dressing until it is healed.

Reduction of Disability

Glenn, Gilbert and Drinker,⁴ have shown that the subcutaneous swelling of burns of the paws can be safely prevented in dogs by the application of plaster. Levenson and Lund¹⁶ applied this method to burned hands, and believe that the motion in burned fingers returns more rapidly to normal after this treatment than it does in cases treated by methods that do not prevent swelling. McClure,²³ in an excellent paper on the treatment of ambulatory burns, shows the value of a simple ointment dressing infrequently changed in reducing the amount of time lost from employment.

TREATMENT OF MAJOR BURNS

When large areas of skin are burned, the situation is complicated by the systemic effects of the burn. These are, according to Wilson, MacGregor and Stewart,²⁴ in order of occurrence, shock,

toxemia and infection. The indefinite term "toxemia" is avoided in this review, and the various manifestations frequently discussed under it are considered separately. Shock in burns is usually caused in large part by a great reduction in the circulating blood volume, which is generally accompanied by hemoconcentration. Other complications of severe burns are, in the usual order of occurrence, hemolysis of red cells and hemoglobinuria, azotemia, azoturia, hypoproteinemia and anemia. Infection is manifested by the usual systemic signs of infection and sometimes by anemia, hypoproteinemia and weight loss.

Shock

The preventive or therapeutic treatment of shock must precede or accompany surface treatment. To treat it intelligently, the hemoglobin level or the hematocrit must be determined at the earliest moment, since changes (concentration of red cells) frequently occur long before changes in the pulse or blood pressure and may therefore give warning of impending serious collapse.

Treatment with blood plasma is by far the most valuable procedure. Saline solution, saline and glucose solution or distilled water and glucose should be given cautiously in the first twenty-four hours^{25, 26} — not for the treatment of shock but to make up calculated losses of electrolyte occurring as a result of vomiting and exposure and from the collection of extracellular fluid in the burned area. Plasma was given by Cope and Rhineland²⁷ in doses of approximately 500 cc. diluted with an equal amount of saline solution to each 10 per cent of surface area burned. Others²⁸⁻³⁰ have used twice this quantity of undiluted plasma. In any case, however, repeated hematocrit determinations should be made to adjust the dosage. If hemoconcentration is present, about 500 cc. of undiluted plasma is suggested for each ten points the hemoglobin level is above 105.⁷ That the treatment of shock with plasma should be started *early*, as stressed by Elkinton,³⁰ has been confirmed by Taylor et al.²⁹

Cortin and other suprarenal substances have been extensively used in the treatment of burn shock.^{9, 31} Cope and Rhineland²⁷ did not find cortin useful in 2 cases. Rhoads and Lee³² now state that further experimentation has made it impossible for them to evaluate cortin because of the inconsistent reactions they have obtained. Morphine has had a traditional and important place in the prevention and treatment of burn shock, and many authors have recommended large doses. In the unusual cases from the Coconut Grove disaster, it was found that large doses of morphine were harmful.³³ Even in the absence of

associated pulmonary lesions, a more cautious use of this powerful drug should be made than has frequently been advised in the past. Tissue anoxia is a large factor in the harm from shock. Since morphine sedation may increase the degree of anoxia, it may be harmful.²⁰ Anesthesia was used by Clowes¹⁰ in the early part of his study, as it has frequently been in the past by other workers, to permit more careful cleaning of the surface. Again, there is serious question of its safety because of the danger of increasing the anoxia. During their more recent cases, Clowes and his associates have omitted the anesthesia. As seen below in the section concerned with surface treatment, the types of treatment in which anesthesia is necessary are no longer those of choice. Although there are no new observations reported on the subject to date, the caution of Blalock³⁴ regarding the danger of overheating in shock should be taken seriously. The patient with a large burned area and a bulky dressing may have been deprived of more than half his normal ability to lose heat by perspiration.

Other Complications

Hemoglobinemia and hemoglobinuria have been known for many years to occur in occasional cases of very extensive deep burns. Shen, Ham and Fleming³⁵ have recently studied this condition and have concluded, as has Drinker³⁶ from animal experiments, that the hemoglobin is derived from blood cells lysed by burning within the capillaries and other vessels of the burned skin and subcutaneous tissues. In occasional cases the excretion of hemoglobin is so rapid that damage arises from the passage of hemoglobin and from its precipitation in the kidney tubules in the usually acid urine. Repeated 4-gm. doses of alkalis (sodium bicarbonate or sodium lactate) are therefore indicated in such cases. Methods of calculating the doses are described by Levenson, Lund and Taylor.²⁹

The development of hypoproteinemia a few days after a severe burn has been recognized for years. Whole-blood transfusion was the only treatment for this condition until recently, when plasma transfusion became available. Neither of these is effective for this complication unless exceedingly large doses are given. Taylor and his associates^{37, 38} have shown that the use of plasma or whole blood for hypoproteinemia is impractical because of the enormous amounts that are needed to overcome the protein deficit. They found that in extreme cases 300 gm. or more of protein or the equivalent of this amount in amino acids must be given daily in addition to an ordinary high-protein

diet. To accomplish this result with plasma would require more than 4000 cc. per day.

In the first few days after a burn, a marked azotemia and azoturia^{37, 38} may occur. Cope and his co-workers³⁹ did not find that this was severe in degree and noted little relation to the severity of the burn. Only one of their cases, however, had an area of more than 10 per cent of full-thickness skin loss. Taylor,³⁸ working with a much larger number of more severely burned patients, found a direct relation to the severity of the burn. This nitrogen is found both in the plasma and in the urine largely as undetermined nitrogen. There is no specific treatment for this condition, but early establishment of adequate urine output is indicated.

Anemia has always been recognized as a complication of severe burns. No treatment save whole-blood transfusion has been effective. In some cases, twenty-five or more transfusions may be needed during a period of two to six months.^{27, 37}

Cope, Nathanson and their associates³⁰ also studied the 17-ketosteroid excretion of burned patients and found that this was depressed in inverse relation to the growth of abnormal amounts of hair on the faces and extremities of female patients. There was also cessation of catamenia for several months.

Infection

In his report of the results of work done by a large number of clinics investigating wounds and burns under the auspices of the National Research Council, Meloney⁴⁰ states, "The infection rate in burns is very disturbing, particularly in deep second and third degree cases." His statistics have not been studied in all useful aspects, but they show in general that large or deep burns have three times the incidence of serious infection that small or superficial burns have. It is difficult to estimate just what this means, because the term "serious infection" is not defined. Clowes¹⁰ showed that all patients with full-thickness burns covering 10 per cent and over of the total surface area were infected with a mixture of organisms and were seriously ill irrespective of which one of three original surface treatments was used. His treatments were tannic acid-silver nitrate, triple dye and vaseline gauze. He also showed that part-thickness burns irrespective of the surface area involved or of the treatment had no serious infection. Full-thickness burns covering up to 10 per cent of the total surface area had numerous infections, but they were relatively easy to control.

As shown by Lyons⁴¹ and Meloney,⁴⁰ cultures from burns usually show mixed infections.

Staphylococci are almost always present in the cultures, and frequently streptococci, colon bacilli, *Pseudomonas pyocyaneus* and various anaerobes are present. No antiseptics, new or old, can control these infections for a long time, but they may reduce the toxicity and invasiveness of some of the organisms. In some cases they may improve the degree of infection enough to allow earlier skin grafting.

Surface Treatment

As indicated in the general outline of the National Research Council,¹ a strong trend away from escharotic treatments prevailed in 1941 and 1942 in the United States and Great Britain. In 1943 this trend has continued and has become more marked.

Tannic acid. Evidence that tannic acid may be toxic to the liver has been increased this year by the paper of Erb, Morgan and Farmer,⁴² who studied autopsies on 61 cases. They found evidence of central necrosis of the liver in 25 of 41 patients dying after tanning, whereas no case of liver necrosis occurred in the untanned patients who died. On the other hand, they point out many real benefits that have arisen from tannic acid treatment. In a clinical paper published in the same month, Farmer⁴³ still advocated this treatment. One of the patients dying of burns in the Boston City Hospital in 1942 who was treated with tannic acid and silver nitrate had central necrosis of the liver at autopsy, but there was also so much pulmonary injury that the liver injury was not the only factor in the death. The British forces in the Middle East had such poor results with tannic acid treatment that they gave it up early in 1942.¹⁷ Their difficulty, however, was infection in third-degree burns. If the alternative to tannic acid treatment were the type of ointment dressings and care given to the average case so treated a few years ago, there would be no doubt that tannic acid, in spite of the real danger of poisoning, would be the better of the two treatments. But if ointment is used with presure dressings or casts, and if proper attention is paid to all the phases of the patient's condition, the evidence is strong that ointments are better. Clowes, Lund and Levenson¹⁰ have presented comparative data on this and two other forms of treatment that suggest that in their series vaseline gauze or triple dye was somewhat safer than tannic acid and silver nitrate.

Triple dye. Triple dye escharotic treatment has numerous strong advocates.^{44, 45} In comparison with tannic acid, an eschar is formed more slowly and usually remains slightly more flexible. In spite of the fact that the dyes are antiseptics, in-

fection always extends under these eschars when those of full-thickness burns are separating. In fact, Aldrich⁴⁴ asserts that such infected areas should be unroofed and redyed daily. This treatment was used extensively at the Boston City Hospital from 1935 to 1942 and was used on a large number of the cases from the Cocoanut Grove disaster.¹⁰ There is no report of toxic damage to the liver as a result of the treatment, but some burns may not heal so rapidly as do those with other forms of treatment.¹⁰

Sulfonamide applications. Sulfanilamide, sulfathiazole, sulfadiazine and sulfaguanidine have all been used in burns in various manners. There are sprays, such as Pickrell's,^{46,47} preformed membranes, such as those of Andrus,⁴⁸ Skinner¹⁹ and Clark,⁵⁰ and ointments, such as those used by Dragstedt¹⁵ and by Gurd.⁹ Sulfonamides have also been dusted on the burn and covered with an ointment. There are reports, however, of very high blood levels with toxic manifestations when the powdered drug has been used in this manner in large-area cases.¹⁷ Gurd⁹ studied the absorption of so-called "micro" crystals of sulfathiazole from a creamy ointment in his cases, and found that high blood levels did not occur in them in spite of high tissue levels on the burn surface.

Propamidine. Propamidine is 4:4' diamidino diphenoxypropane dihydrochloride, which is an aromatic diamidine possessing well-marked activity against various protozoal organisms as well as against the gram-positive cocci.⁵¹ It is of interest because its action is not inhibited by para-aminobenzoic acid as is that of the sulfonamides. As yet there are no published American studies on the use of this material, but there are several British reports.^{19, 52-54} To date it has been used mostly on minor burns, and the reports indicate some antibacterial activity. Healing takes place about as rapidly as with other nonescharotic treatments.

Penicillin. The only British report¹⁹ on penicillin showed a favorable antibacterial action. The single American paper⁴¹ was rather guarded in its claims because it was given to patients at the same time that sulfadiazine was being used.

Pressure dressings. Bulky dressings with more or less pressure are being used in major burns by Allen and Koch,²⁰ Siler and Reid,²¹ Owens,²² Cope,¹⁵ Gurd⁹ and Clowes.¹⁰ Five of the six papers report cleaning of the wound before dressing it, but Cope did aseptic dressings without preliminary cleaning. In three reports, boric acid ointment^{15, 20, 21} was used under the dressing, and in one each, sterile saline solution,²² sulfathiazole ointment⁹ and sterile vaseline.¹⁰ Sulfadiazine was usually, but not always, given by mouth.

Plaster casts. Trueta,³ Barnes,⁵⁵ Roulston,⁵⁶ Cohen,⁵⁷ Logie¹⁷ and Levenson and Lund¹⁶ have all used plaster casts as a primary treatment in major burns. This treatment is not new, having been previously recommended by Zeno⁵⁸ and Afonso.⁵⁹ The important experiments of Glenn, Gilbert and Drinker⁴ and of Barnes and Trueta,³ however, have placed this treatment on a firm scientific basis and have shown that the cast should fit closely and should be closed over the end of the extremity. Its most essential feature is that it prevents swelling and decreases the abnormally high flow of lymph that occurs in a limb that is not protected by a cast. Under these circumstances, the bacteria present on the surface become relatively harmless. Logie¹⁷ says: "The three burns I was able to culture at the end of a fortnight, when the plaster of Paris was removed, grew hemolytic streptococci, and this occurred despite the usual course of prophylactic sulfonamide by mouth. But neither the patient nor the burn seemed to mind."

Secondary treatment. Any secondary treatment that entails frequent changes of dressing may expose the patient to the danger of introduction of new strains of pathogenic organisms. Owens²² leaves his primary treatment in place for three weeks or more, and when he removes it from deep burns he wipes off the pus and debris and immediately covers the granulations with a Thiersch skin graft. In this way he avoids unnecessary contamination.

The only other relatively new secondary treatments concern the employment of new chemicals, such as propamidine and penicillin, as described above, and the use of the Bunyan⁶⁰ bag for saline irrigation. Clowes¹⁰ found the bag useful in the few cases in which it was tried, whereas Cannon⁶¹ did not. The trend of opinion is that infrequent dressings, simple applications and careful asepsis are the most important considerations in the surface care of burns during the time when areas of third-degree burn are being prepared for grafting.

SKIN GRAFTING

It is easy to say that early grafting should be done, but it is sometimes extremely difficult to get the patient into condition for such grafting. Rampant infection, anemia, hypoproteinemia and possibly vitamin deficiencies⁸ all prevent technically perfect grafts from taking. Clowes¹⁰ has shown that infection per se does not prevent the success of a graft if the nutritional status of the patient is in fair balance.

The technic of skin grafting is unchanged. More emphasis is placed on early grafting to avoid the thick scars that follow late grafts. Split-

thickness grafts, sewed into place under slight tension, have almost entirely displaced Reverdin grafts in the best clinics,^{7, 81} but there are a few desperately sick patients that can be grafted only by the Reverdin method.¹⁰ The Padgett dermatome is widely used to cut split grafts. Cannon⁶¹ successfully used an interesting type of abdominal flap very early in a case with total destruction of the skin of the dorsum of the hand and partial sloughing of the extensor tendons. In addition to Cannon's paper, the article on grafting in Volume V of *Military Surgical Manuals*⁷ is extremely useful.

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ing to the lower lobe." In other words, this child had an atelectatic lower lobe without infection in the bronchi or in the pleural fluid surrounding the atelectatic lobe, and neither could be true if the atelectasis were secondary to intrinsic bronchial obstruction or infection, as productive bronchiectasis and empyema would surely have followed. Also, the collapsed lobe was in the midchest rather than in the posterior gutter, where intrinsically collapsed lower lobes are found. The final clue to the reason for compression atelectasis is given in the x-ray demonstration of a well-defined mass in the posterior portion of the right chest.

The differential diagnosis on admission of the patient to this hospital, at the age of six and a half, after an illness of at least six years, should furnish the answer to three simple questions: What kind of tumor was it? Where had it originated? and Why?

By exclusion, it was not a tuberculous abscess because of two negative tuberculin tests and no signs of tuberculosis elsewhere in the body. It was not a pyogenic abscess because all indications of systemic reaction to pyogenic infection were lacking. It was not a lesion of the adrenal gland because the blood pressure was normal and it had grown too large.

This lesion had grown in such a location and tissue plane that it pushed the liver and duodenum forward and to the left, the hepatic flexure downward and to the left and the right kidney downward and backward and that it penetrated the diaphragm and collapsed the lower right lung, displacing it forward and to the left. In other words, it lay in the right paravertebral gutter and in the retroperitoneal tissue plane.

The retroperitoneal tumors in this location that must be considered in this case include only the group derived from tissue elements of the embryonal urogenital ridge. They are carcinoma and hypernephroma of the kidney, embryoma, Wilms's tumor, ganglioneuroma and teratoma. Except for passive hydronephrosis from positional displacement, the data of the case afford no evidence of renal disease and establish the fact that the tumor had existed for five and a half years. For these two reasons carcinoma and hypernephroma of the kidney are untenable diagnoses.

Every feature of this lesion classifies it as an embryoma, using the term in its strict dictionary meaning of a tumor derived from embryonal structures. I should perhaps refresh your memory that the embryonal structures are those which exist during the embryonal stage, and that this stage refers to the product of conception from the end of the second to the beginning of the eighth week of its intrauterine existence. Such tumors tend to grow to enormous size, to show calcification with-

in their substance, as a result of hemorrhage infection or necrosis, and to usurp by displacement and pressure rather than invasion the space allotted to normal organs. Derived from embryonal tissue, they possess the abortive but nevertheless potential growth capacities of the three primordial germ layers, and express the attempt to produce organ facsimiles of their host with variable completeness of frustration and confusion. Any tissue may be represented except true genital cells. Ganglion cells are frequently numerous, and if nonmedullated, irregularly coiled masses of nerve fibers predominate, the tumor is given a sub-name of ganglioneuroma. If renal and striated muscle cells fill the pathologist's microscopic section and the host, usually a child, has died within two years from metastasis of a carcinoma developing in some point of the tumor epithelium, it is called a Wilms's tumor. This is not, therefore, a Wilms's tumor. If the specimen includes developmental products of independent or aberrant germ cells recognizable as rudimentary organ masses, it is called a teratoid tumor or teratoma. It would be futile for me to try to classify this tumor beyond the term embryoma.

If analogy from experiments on parthenogenesis in frog ova, asymmetry reversal in *Patiria* blastulae, polyembryony in nine-banded Armadillo ova, and deductions from human instances of situs inversus, twinning and monstrosity are correct, tumors of this sort result from temporary disruption of normal intrauterine environmental factors at a critical period of development, whereby a mass of embryonal cells is separated from its fellows, and later produces an embryoma through parasitic growth.

DR. EDWARD B. BENEDICT: How do you explain the lesion involving the chest as well as the abdomen?

DR. ADAMS: I¹ reviewed this subject six years ago and I have not had a chance to look into it since. Mall,² MacCallum,³ Newman⁴ and notably Bosaeus⁵ described tumors such as this, and in the lower animals those arising from the urogenital ridge often occupy both pleural and abdominal cavities. I think this tumor has expanded through the diaphragm.

DR. BENJAMIN CASTLEMAN: Do you want to go any farther and say whether you think the tumor is benign or malignant?

DR. ADAMS: I have gone quite far already. If it is an embryoma in the strict sense of the word or, to specify further, if it is a teratoma, it is a benign lesion; but having the three primordial germ layers originally present, it could become malignant. MacCallum had a patient with true teratoma who finally died of metastases, and it

was found post mortem that the metastasis was from a carcinoma that had developed within the teratoma and that blood-vessel emboli were the source of the metastatic growth.

DR. CASTLEMAN: Such a condition is occasion-

abdomen primarily, we should also have been in trouble.

We waited forty days and decided ahead of time to go into both places. An incision was made between the scapula and the spine, down



FIGURE 1. Roentgenogram of Chest and Abdomen.

The upper arrow points to the lipiodol injected into the mass within the chest; the lower arrow, to areas of calcification within the area of radiolucence.

ally found in the ovary and in teratomas, that is, the part that becomes malignant is usually the epithelial element.

DR. ADAMS: This tumor had not been malignant during the six known years of growth. I do not know how I could say whether eventually it showed malignancy in some one of its parts.

DR. RICHARD H. SWEET: I should like to say that it took us forty days to come to the conclusion that Dr. Adams has reached in a few minutes. I must confess that our approach was not so philosophic and certainly not so poetic; in fact it was very practical because I wanted to know where to make my incision. It turned out that if we had gone into the chest primarily, we should have been in trouble; if we had gone into the

through the ninth interspace, across the costal margin into the right rectus sheath and down the rectus sheath to a point below the level of the umbilicus. The abdominal portion of the incision was opened first, and the tumor was found lying retroperitoneally between the kidney and the liver. On incising overlying peritoneum, it was soon discovered that the tumor passed directly through the diaphragm. The incision was therefore enlarged by dividing the eighth, seventh and sixth ribs posteriorly. The attachments of the tumor to the diaphragm were then divided and the abdominal portion was freed. It was most adherent to the sides of the vertebrae, at which point great care had to be exerted to avoid the vena cava. There were several large branches of the intercostal ar-

teries going directly onto the tumor at this point. After freeing the abdominal portion and dividing the rim of diaphragm that surrounded the tumor, the dissection was carried up within the chest where the tumor was found to be cystic. That is what had been tapped all these years. The largest portion of the tumor lay within the chest, and it was adherent to the parietal pleura, to the under-surface of the right lower lobe of the lung and to the pericardium. All adhesions were separated by blunt dissection without much difficulty. The tumor was finally removed in one large dumbbell-shaped mass.

CLINICAL DIAGNOSES

Tumor of chest (? cyst).
Dermoid cyst of abdomen.

DR. ADAMS'S DIAGNOSIS

Embryoma of retroperitoneal space, with extension through the diaphragm into the chest.

ANATOMICAL DIAGNOSIS

Dermoid cyst of chest, abdomen, retroperitoneal space and postero-inferior mediastinum.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: This tumor was filled with large amounts of sebaceous material; the wall was in places hard, fibrous and cartilaginous, and in other places calcified and ossified. It had all the characteristics of what we ordinarily call a dermoid cyst or that type of embryonal tumor that is made up for the most part of skin, sebaceous glands, hair follicles, calcium, cartilage and bone, and that fits in with Dr. Adams's diagnosis of embryonal or teratoid tumor.

The patient went back to Nebraska and is now well, four months after discharge.

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CASE 29482

PRESENTATION OF CASE

A forty-one-year-old unmarried woman, a factory worker, entered the hospital because of pain and marked swelling in the left foot.

At the age of seven years the patient developed multiple bony swellings usually preceded by "hot and searing" pain. From about the age of fourteen her general growth and physical development appeared considerably retarded. Slow growth was also noticeable in the various bony swellings to such an extent that the onset of a tumor in her finger, which at the time of entry markedly interfered with her activity, could not be remembered. The swellings, however, were always preceded by the sensation already described. Six years before entry she noticed weakness in the left ankle. This was followed in a few weeks by the hot-and-searing sensation. A small fusiform swelling appeared on the distal part of the tibia, which progressed slowly. One year prior to admission the swelling in the ankle became quite large and painful. She was admitted to a community hospital where x-ray films were taken and the tumor was removed. About six months later the swelling in the left ankle recurred and became more painful.

Her mother was said to have had "arthritis" in one knee. Five brothers and one sister were well developed and of normal height.

Physical examination showed a dwarfish woman, who was 52 inches tall. There was a left total curve of the spine. The right scapula was lower and more prominent than the left. The spinal motions were "good." There was considerable flaring of the right costochondral margin, and atrophy of both pectoral muscles. Multiple small nodules were present on the distal ends of the right radius, ulna and proximal phalanx of the thumb. Similar nodules were present in the middle phalanx of the left middle finger and in all the phalanges of the fifth finger. There was only minimal motion of the interphalangeal and the metacarpophalangeal joints but full range of motion in the other joints. The right anterior superior spine and the iliac crest were much more prominent than those on the left. A nodule was palpable in the right iliac crest. On the medial aspect of the left ankle, extending anteriorly and over the lateral side, with considerable gross deformity of the foot, was a mass about 10 cm. in diameter, which was hard and covered with tensely stretched, warm, slightly reddened skin. There was no motion in the left ankle. There were multiple small nodules on the left tibia and the lower aspect of the left femur, the phalanges of the second and third toes, and the adjacent metatarsal bones. The right lower extremity showed posterior bowing of the fibula, with multiple small palpable "bony masses" on the proximal aspect of the tibia and a small one on the distal portion of the femoral shaft. There were many small nodules on the phalanges of all the

toes of the right foot. The ankle motion was normal.

The blood pressure was 120 systolic, 50 diastolic. The temperature was 98.6°F., the pulse 86, and the respirations 20.

Examination of the blood showed a red-cell count of 3,860,000, with 70 per cent hemoglobin.

merous areas of calcification. The lower end of the left tibia was irregularly destroyed, and there was a grapefruit-sized soft-tissue tumor with areas of calcification and bone fragments within it that replaced the os calcis and talus (Fig. 1). There were numerous cyst-like expanding lesions in the bones of the hands (Fig. 2). A lateral film



FIGURE 1. Roentgenogram of Left Ankle.

The white-cell count was 5500. A blood Hinton test was negative. The urine sediment contained 10 epithelial cells per high-power field, and the urine gave a ++ Sulkowitch test for calcium. The sedimentation rates were 2, 12, 23 and 32 mm., respectively, at fifteen-minute intervals. The blood calcium was 10.5 mg., the phosphorus 3.8 mg., and the phosphatase 6.4 Bodansky units per 100 cc.

X-ray examination showed the bones of the lower legs to be shorter than normal. At the ends they were irregularly widened with multiple cyst-like expanding lesions. The bone structure at the ends of bones was irregular, and there were nu-

merous areas of calcification. The lower end of the left tibia was irregularly destroyed, and there was a grapefruit-sized soft-tissue tumor with areas of calcification and bone fragments within it that replaced the os calcis and talus (Fig. 1). There were numerous cyst-like expanding lesions in the bones of the hands (Fig. 2). A lateral film

of the skull showed a cyst-like area projected on the sella, but no other significant findings were present. There were no metastatic lesions in the chest; the costochondral junctions were irregular and widened with areas of calcification in poorly defined rib ends, which merged with the calcified costal cartilages.

On the third hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM BECKMAN: The essential features of this case—the bony nodules or lumps on the bones that developed progressively from child-

hood and were still developing at the age of forty-one, the short stature of the patient and the deformity of the skeleton, that is to say the bowed legs and the curved spine—constitute a syndrome that has been well recognized by the medical profession since at least the late eighteenth century. This is a syndrome called by many names, of which the commonest are multiple cartilaginous



FIGURE 2. Roentgenogram of Left Hand.

exostosis and multiple enchondromatosis. The way I was able to make the diagnosis was to take the x-ray films and look through an x-ray textbook until I encountered other ones like them. Then there was no question that it represented a characteristic syndrome. I think that Dr. Schulz might describe the x-ray findings at this time.

DR. MILFORD SCHULZ: Primarily, this patient shows a dysplasia of chondral bone growth. That portion of the bone involved in periosteal and endosteal growth is not particularly disturbed, but where this meets the epiphysis there is disruption of the normal character of the bone. These portions are wide, short and deformed. Here in the chest the costochondral junctions show severe deformities with irregular areas of calcification with-

in them. These lesions in the hands, of course, are quite characteristic of multiple enchondromas. You might be interested in seeing the films that were taken at the community hospital six years before entry. There was then only a small amount of calcification in the soft tissues around the ankle. Now the talus and calcaneus are destroyed, and the tumor has involved and destroyed the lower end of the tibia.

DR. BECKMAN: Another feature of this disease is that the bones are affected irregularly. That is particularly apparent in this case if you compare the metacarpal bones in the two hands. It can be seen that the corresponding bones are not always of the same length.

I have tried hard to work out a differential diagnosis because that is what one is supposed to do at these exercises; but it is difficult because there is nothing else that looks like this. I found one case that had been confused with hyperparathyroidism, but certainly this could not be considered here, particularly since there was no alteration in the blood chemistry.

Honeij¹ did metabolic studies and found that patients with the syndrome under consideration excrete more calcium on a low-calcium diet than an ordinary person does; but these experiments were repeated by Sanderson and Smyth² who found no deviation from normal. Hence, there is probably no disorder in the calcium metabolism. In 1917 a report by Ehrenfried³ from the Children's Hospital states that there were 600 cases in the literature at that time. Thus it is not so rare a condition as it might seem. The disease is usually hereditary, and in one family of seventy-six members, twenty-two of them were afflicted. This patient knew of no signs of the disease in any of her family so the hereditary aspect was not present, which is true in about one third of the reported cases.

One significant clinical datum was omitted when they did not tell the duration of the chief complaint but I assume from the story of the present illness that it was probably six months or so. At any rate it is quite evident that something different was going on in the left ankle.

It is unusual to have pain in benign tumors, and although this patient always had pain, it never bothered her enough to go to a hospital. Then, because of severe pain in the ankle she sought medical advice. The tumor in the ankle was also different because it grew much faster than the others, and six months after removal it had recurred. Also, the soft-tissue reaction around the ankle with redness and heat was different

from the changes observed during the development of the other swellings. Furthermore, she had evidence of constitutional disease, as shown by an elevated sedimentation rate and anemia. She also had a slightly elevated phosphatase, which suggests that osteoblastic activity was vigorous. I believe that one of the enchondromas in the left ankle had become malignant and that an amputation was performed.

DR. BENJAMIN CASTLEMAN: When you say "enchondromas," are you making any distinction between osteochondroma and enchondroma?

DR. BECKMAN: No, although I probably should have. Both are present in this disease. You can see all sorts of little ones in the phalanges—enchondromas and exostoses.

DR. CASTLEMAN: Dr. Schulz, will you comment on that? Are these tumors osteochondromas or enchondromas? I think there is a definite distinction.

DR. SCHULZ: I do not know whether one can classify them as exostoses or enchondromas. Those in the hands, of course, are quite characteristically enchondromas.

DR. GEORGE W. HOLMES: I believe that it would be possible for enchondroma to be responsible for the entire picture. A central tumor producing a local expansion of the bone might be projected in such a manner that it would appear to be partially outside the bone. Radiologically the only difference between an enchondroma and an osteochondroma is the location.

CLINICAL DIAGNOSES

Chondrosarcoma of tibia.
Multiple enchondromatosis.

DR. BECKMAN'S DIAGNOSES

Chondrosarcoma of tibia.
Multiple cartilaginous exostoses.
Multiple enchondromatosis.

ANATOMICAL DIAGNOSES

Chondrosarcoma of tibia.
Multiple enchondromatosis.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: There has been a lot of misunderstanding concerning these two diseases.

DR. WALTER BAUER: "Loose talk" is a better term.

DR. CASTLEMAN: First let me define some of the terms that we are all agreed on. We use the terms "exostosis" and "osteochondroma" interchangeably because these tumors appear to project out from the bone and because they are usually composed of both bone and cartilage. These tumors may be either single or multiple, and when

multiple the disease is usually hereditary and called "multiple cartilaginous exostoses" or what Jaffe⁴ in a recent paper prefers to call "hereditary multiple exostoses." Pathologically exostoses may be predominantly cartilaginous or osseous, and occur almost always in the vicinity of the epiphyseal cartilage. According to Jaffe they are covered with periosteum and their outlines are really irregularly outpouched cortex; they are not superimposed on the cortex.

An enchondroma is a cartilaginous tumor inside the bone, often occurring close to the epiphysis, but not necessarily. These tumors may also be single or multiple, and when multiple the condition is often called "multiple enchondromatosis" or, according to Ollier,⁵ "dyschondroplasia." This disease is not hereditary and is sometimes called Ollier's disease. Some of the confusion between this condition and multiple cartilaginous exostoses is due to the fact that Ollier⁶ also published a paper on the latter disease. Ollier, however, made a definite distinction between the two. There is no definite evidence that combinations of the two conditions have occurred in the same patient.

DR. BECKMAN: Ollier described a unilateral disease; Ewing,⁷ however, makes no differentiation between Ollier's disease and the condition present in this patient.

DR. CASTLEMAN: It is true that Ollier first described it as unilateral, and for that reason disease involving both sides was formerly not called Ollier's disease. Usually the lesions are only on one side, but there have been a number of cases reported in which they occurred on both sides. Even Ollier's own students⁸ described them on both sides.

This patient's foot was amputated about 8 cm. above the ankle. The tumor was composed of cartilaginous nodules, and microscopic examination showed it to be a chondrosarcoma. In addition many of the phalanges away from the tumor were almost completely replaced by enchondromas. No exostoses were found. I believe, therefore, that this is a case of multiple enchondromatosis with sarcomatous degeneration of one of the lesions in the lower end of the tibia.

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THE HEALTH OF THE NATION

DURING the one hundred and fifteen years of its existence, the *Journal* has witnessed many changes in medical and public-health practices in the United States, all of which have been directed to the ever-present responsibility of the medical profession—the improvement of the health of the people.

Medical research has steadily advanced knowledge concerning the cause, prevention and treatment of disease. Drugs such as arsphenamine, insulin, liver extract, the sulfonamides and penicillin have been shown to possess phenomenal curative effects. Morbidity and mortality rates have declined to figures that, only twenty-five years ago, would have been considered fantastic. Certain communicable diseases, such as smallpox, typhoid fever and diphtheria, have been practically

eliminated as health hazards. Undergraduate and postgraduate medical education has improved to such an extent that it is unequalled in any part of the world. Hospital facilities in most regions of the country are adequate, regarding both number of beds, trained personnel and equipment.

Other factors that are indirectly concerned with the practicing physician have contributed to the improved health of the people. Measures promoted by public-health departments, such as sanitation, quarantine, tuberculosis case-finding and immunizing methods, have played a significant role, particularly in the control of communicable diseases. The creation of boards and colleges of specialists has led to the recognition of those who are properly qualified in their particular fields. Nationwide programs have done much to educate the population concerning medical matters, and in the majority of states opportunity for budgeting the costs of hospital or medical care, or both, is available.

In spite of all these things that are directly or indirectly concerned with the practice of medicine, a number of nonmedical conditions have influenced the health of the Nation. Among these should be included good wages, a high standard of living, unsurpassed educational facilities, excellent means of transportation, and well-endowed and well-administered charitable organizations.

The total result has been a nation as healthy as, if not healthier than, any other nation in the world, and one whose health is constantly improving, and yet the people of the United States and the medical profession are now faced with a proposed legislative act—the Wagner-Murray-Dingell Bill—that purports to promote an even healthier population by the federalization of many of the activities that have been responsible for the advances of the past and that, by and large, have been the direct result of the essence of democracy—individual enterprise and effort.

Within the past two months officially appointed representatives of the state medical societies of New England have jointly considered what steps should be taken regarding this epitome of bureaucracy. The group drafted a statement con-

cerning the proposed legislation, which is printed elsewhere in this issue of the *Journal*. The statement has been approved by the appropriate executive bodies of the state medical societies, and on December 2, copies were forwarded to each senator and representative in Washington by the medical society of his respective state.

The gist of the statement is a plea for the utilization by the states of existing voluntary agencies, if necessary with the assistance of federal grants-in-aid. In other words, it seems likely, if not inevitable, that federalization of medical and hospital care and of medical education and research would destroy the very foundation on which the health of the people of the United States is based. Certainly the threat is so ominous that every physician should explain to his patients and friends what agencies and philosophies have been responsible for the advances of the past, how these would be affected by the Wagner-Murray-Dingell Bill, and how such uncontrolled and radical experimentation can be avoided.

POSTWAR TUBERCULOSIS CONTROL

THE foundation for ending tuberculosis in the United States, and for its control in all the world, is now being laid in wartime by the United States Public Health Service and the National Tuberculosis Association. The outlook for success is good. This is in face of the fact that, in long wars, tuberculosis has been a prime factor in raising the general death rate. The rise already has come in Europe. Its first signs appeared this spring in the United States, where the general tuberculosis death rate still was falling, but where an upturn came among the young. The small American setback had an ominous counterpart in Europe, where children were affected much more than adults, particularly by the nonpulmonary types of the disease. In England and Wales, deaths among children under ten years of age from all forms of the disease increased 45 per cent during 1941 over the 1939 figure, as compared with a 12 per cent increase for the general population. In Paris during the same period, the death rate among children from one to nine rose 28 per cent, as against only a 10 per cent increase for the

general population. This shows the insidious ways of tuberculosis and the magnitude of the job, because, when this war started, it was expected that those to be the hardest hit would be not British children but young women war workers, who were the foremost victims in World War I. An explanation suggested for the plight of American children is their mothers' diversion to war work.

In World War I, in Germany the tuberculosis death rate rose 61 per cent, in Italy 44 per cent, in England 42 per cent and in the United States 6 per cent. Authentic reports from Germany and Italy have not been available since the start of World War II. Meager reports from France show that deaths from tuberculosis have increased. But England held her increase in deaths from the disease to about 12 per cent during 1940 and 1941, and during 1942-1943 the number of deaths dropped to the 1938 level, which is the lowest on record. The tuberculosis death rate in the United States during a period lacking only a few months of the duration of her participation in World War I was still dropping. The 1941 death rate was an all-time low of 44.4 per 100,000, was probably about 43 for 1942, and this year will undoubtedly be still lower.

There are many angles behind this hopeful side, but the main weapon by which Americans propose to drive tuberculosis from the land is increasing use of x-ray films of the chest. The Selective Service boards and induction stations employ it on draftees, and state after state, and county after county, are following up the men deferred or rejected on account of tuberculosis. The United States Public Health Service and state tuberculosis organizations are extending the use of such films to war industries, and the same follow-up to promote medical care is used as in draftees. Furthermore, the Public Health Service is extending its offer of service to families of workers found to be tuberculous, and the War Emergency Committee of the National Tuberculosis Association has recommended to local tuberculosis associations many measures, including special attention to women employees and to emergency housing conditions.

Tuberculosis is coming to light in a great sector of the population where it was never before searched out on a large scale. The magnitude amounts to something new in this great health battle. The momentum here and in England promises success for the international postwar control activities now planned by the United States Public Health Service and the National Tuberculosis Association. Certainly the annual Christmas Seal Sale, the proceeds of which provide substantial support to this program, deserves the enthusiastic support of every physician!

MEDICAL EPONYM

LIBMAN-SACKS SYNDROME

Emanuel Libman (b. 1872) and Benjamin Sacks (b. 1896) are the authors of a paper, entitled "A Hitherto Undescribed Form of Valvular and Mural Endocarditis," appearing in the *Transactions of the Association of American Physicians* (38: 46-61, 1923). This same article also appeared in the *Archives of Internal Medicine* (33: 701-737, 1924). A portion of the discussion follows:

We have had the opportunity of studying the clinical and pathologic findings in four cases of a hitherto undescribed form of endocarditis, which we have for the present described as an atypical form of verrucous endocarditis. . . .

The disease . . . ran a subacute course, with fever and progressive anemia. Briefly enumerated, the clinical findings were pericarditis, white-centered petechiae, arthritis, erythematous and purpuric rashes, ulcerative lesions of the mucous membranes, pleuropulmonary symptoms, embolic phenomena, enlargement of the liver and spleen, acute glomerulonephritis, a tendency to leukopenia and repeatedly negative blood cultures. Two of the patients had an eruption on the face which resembled acute lupus erythematosus disseminatus. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

WAGNER-MURRAY-DINGELL BILL

The following open letter was forwarded, as of December 2, to all Massachusetts members of the Senate and House of Representatives in Washington. It is expressive of the collective viewpoint of the medical societies of Maine, New Hampshire, Vermont, Massachusetts, Rhode Island and Connecticut regarding Senate Bill 1161 and House Bill 2861—the so-called "Wagner-Murray-Dingell Bill."

MICHAEL A. TIGHE, *Secretary pro tempore*
New England Conference
Wagner-Murray-Dingell Bill

MASSACHUSETTS MEDICAL SOCIETY
8 Fenway, Boston

December 2, 1943

Dear Sir:

The Massachusetts Medical Society, in conjunction with the medical societies of Maine, New Hampshire, Vermont, Rhode Island and Connecticut, has studied Senate Bill 1161 and House Bill 2861 now before the Congress of the United States and respectfully submits its views on this proposed legislation.

We approve of the broad medical objective of the act that we interpret to be an attempt to improve the health of the people. As a basis of our approval we cite the progressive leadership which the physicians of New England have always shown in the development of public-health enterprises. For more than fifty years we have consistently supported the plea for the establishment of a National Department of Health with a secretary in the President's Cabinet, under whom would be co-ordinated many important public-health programs, exclusive of the Army and Navy. These are now scattered through various departments and bureaus of the federal government and already play a large role in the provision of medical care for the people of this country.

We approve of the use of the insurance principle on a voluntary basis as a means to aid the individual to budget against the cost of medical care. We maintain that when insurance programs are not directly under the supervision of the medical profession by whom medical care is to be rendered, they should provide for cash benefits to be paid to the individual, for we firmly believe that the citizens of New England are capable of using cash benefits to pay the costs of medical care.

We believe that S. B. 1161 and H. B. 2861 do not provide for the sound development of a national health program. It is implied by the act that the distribution of compulsory savings managed by federal authorities will guarantee better health for all the people. We sincerely doubt that such an objective can be realized in this way. In the New England states, judged by any standards with which we are familiar, there is no need to revolutionize the habits of the people in their methods of obtaining medical care.

Private enterprises in the field of voluntary prepaid medical and hospital insurance are increasing rapidly. *These facilities should be utilized by the states, if necessary through federal grants-in-aid, so that each state can purchase medical care for those who cannot purchase it for themselves.* This we believe to be a development that would be acceptable to the New England people, for thereby medical care could be provided even for the indigent who are public charges, a provision most desirable in those communities that have been unable or unwilling to meet this obvious responsibility.

We shall be glad to work out plans with representatives of the federal and state governments to improve the health of all the people, but we should expect that any plans that might be devised would take full advantage of existing agencies and be developed within the social patterns that are well understood by our people.

Very truly yours,

[Signed] Roger I. Lee
ROGER I. LEE, M.D., *President*
[Signed] Michael A. Tighe
MICHAEL A. TIGHE, M.D., *Secretary*

(Notices on page xiv)

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STUDIES IN DIABETES MELLITUS AND TRANSIENT GLYCOSURIA IN SELECTEES AND VOLUNTEERS

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WITH THE ASSISTANCE OF SERGEANT LOWELL V. KINGSLEY, A.U.S.

BOSTON

A FEATURE of the medical examination of selectees and volunteers at the Boston Armed Forces Induction Station has been the frequency with which glycosuria was discovered. Since most studies in diabetes mellitus have been made on more or less select groups of people, few of them give a clear idea of the frequency and significance of mellituria in a cross section of the population. The incidence of the disease has been based on life-insurance examinations, mortality statistics and various surveys. Limitations of such results are obvious, and calculations from mortality figures are crude. Consequently, considerable variations in the frequency of this condition have been reported.

A most interesting large-scale survey of the occurrence of known diabetes mellitus in the general population was made under the direction of the United States Public Health Service¹ in 1935-1936. The results were based on a house-to-house canvass of some 800,000 families, which included 2,800,000 persons. It was estimated from this survey that there were 660,000 cases of diabetes mellitus in the United States. This figure, however, represented only known cases of diabetes, and no doubt there were many unrecognized ones in the population studied, as can be inferred from the number of unrecognized cases discovered in the present study. A report of the medical findings in the New York City Selective Service Administration showed the incidence of diabetes to be 416 cases (0.36 per cent) among 155,569 registrants in the City of New York.²

The majority of observations of the various phases of this disease have been made on cases of diabetes with symptoms in groups of people that are not representative of the male population. Consequently, not so much is known about the cases of diabetes that have been found on routine exam-

inations. The opportunity presented itself to study at the Boston Induction Station various aspects of transient glycosuria and diabetes and their relation to socioeconomic factors in a large unselected group of men. In this group, an estimated 78 per cent of the cases of diabetes were discovered without the persons' ever having known that they had the disease. It seemed that an investigation of such cases of diabetes as well as those of known duration would be of considerable significance.

This paper presents a study of diabetes mellitus and transient glycosuria in 45,650 consecutive selectees and volunteers, aged eighteen to forty-five years, who appeared for final examination at the Boston Induction Station, prior to induction in the armed forces. The men appearing for final examination at this station form an excellent cross section of men of military age without dependents, not engaged in essential industry, and not possessing obvious disqualifying defects evident on inspection by local-board examiners.

PLAN OF INVESTIGATION

All men had thorough physical and mental examinations, routine chest roentgenograms and urine examinations.

The test for sugar in the urine was made with Benedict's qualitative solution. The qualitative amounts of sugar in the urine were indicated according to the color changes: + for green, ++ for yellow, +++ for orange and ++++ for brick red. When sugar was found, the urine was tested again before and after lunch on the same day. If the repeated urine examinations showed sugar and if there was not a verified history of diabetes, the men were sent to an Army hospital for sugar-tolerance tests. A standard dose of 100 gm. of dextrose was employed and was ingested after the subject had fasted overnight. The con-

centration of sugar in the blood and urine was determined in specimens taken during fasting and at intervals of one half, one, two and three hours after the ingestion of the dextrose. The determination of the blood sugar was made on 2-cc. samples of venous blood according to the method of Folin and Wu.³

Observations were made on certain clinical and social aspects of diabetes mellitus and transient glycosuria. The clinical aspects studied were incidence and diagnosis, age at onset and at present, height and weight, frequency of hypertension and of pulmonary tuberculosis, general physical status and family history of diabetes. The social investigations consisted of community studies on the relation of the prevalence of diabetes mellitus to socioeconomic level, community welfare rate, population density, occupation and nationality. All cases of diabetes were classified according to the type of community from which they came. The social study of these communities was made according to the plan of Hyde and Kingsley.⁴ Their classification of community socioeconomic level was based on good, medium and poor community desirability. These findings were compared with those of a large control group of nondiabetic persons who were examined here.

INCIDENCE AND DIAGNOSIS

The incidence of glycosuria, which in degree varied from + to +++++, was found to be 367 cases (0.8 per cent) of the 45,650 men examined. For the purpose of simplicity the cases of glycosuria were divided into three groups, as follows: 208 cases of diabetes mellitus, 126 cases of transient glycosuria, and 33 cases of renal glycosuria, which have been reported elsewhere.⁵

Diabetes mellitus was diagnosed when the subject had a blood-sugar concentration that reached a level of 180 mg. per 100 cc. and some or all of the urine specimens contained varying amounts of sugar after the ingestion of 100 gm. of glucose. Some of the fasting urine specimens were sugar free and some of the fasting blood sugars were normal. Of the 208 cases of diabetes mellitus, 107 were mild, 58 were moderate, and 43 were severe. Illustrations of these are given in Figure 1.

The cases of mild diabetes usually showed normal fasting blood-sugar levels. Some of the fasting urine specimens contained sugar, whereas others were sugar free. After the ingestion of the test dose of glucose, the blood sugar rose in one half or one hour to 200 or 220 mg. per 100 cc., and then dropped in two hours to 150 mg. and in three hours to 100 or 125 mg. The urine specimens contained varying amounts of sugar.

The moderate cases of diabetes showed a fasting blood-sugar level of 140 mg. per 100 cc., with or without sugar in the fasting urine specimens. After the ingestion of the glucose the blood sugar rose in one half or one hour to 275 mg., and then

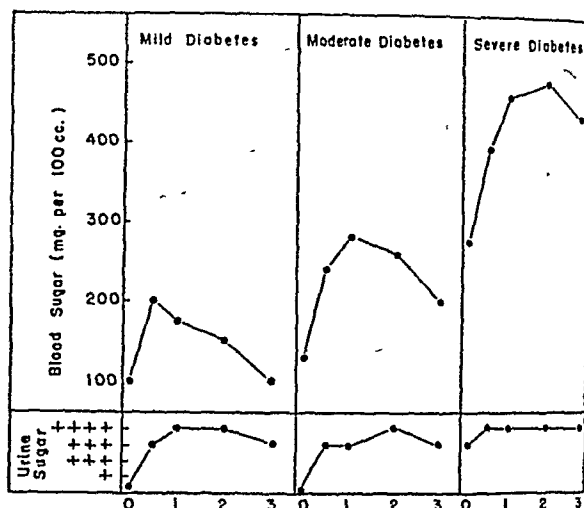


FIGURE 1. Characteristic Results in Mild, Moderate and Severe Diabetes Mellitus at Hourly Periods after the Ingestion of 100 Gm. of Glucose.

dropped to about 200 mg. in three hours. The urine specimens contained varying amounts of sugar.

The cases of severe diabetes showed a fasting blood-sugar level of 275 mg., with considerable amounts of sugar in the urine. After the ingestion of the glucose the blood-sugar level rose to about 475 mg. in one hour and dropped only slightly in three hours. All the urine specimens contained large amounts of sugar.

Transient glycosuria was diagnosed in the men who had varying amounts of sugar in the first specimen of urine tested, and showed negative reactions on subsequent tests during the day. If sugar-tolerance tests had been done in all these cases, it is quite probable that a number of cases of diabetes mellitus and renal glycosuria would have been discovered.

CLINICAL FEATURES

Age. Diabetes mellitus may be recognized at any period from infancy to old age. Although the men examined here were over eighteen years of age, a number of them knew that they had had the disease since childhood.

The incidence of glycosuria at the various present ages and the age at onset are given in Table 1. It shows that the average age of the diabetic patients was 34.4 years, that of the men with transient glycosuria 30.9 years and that of the control group 27.5 years. Ordinarily one thinks of the

severe cases of diabetes as being in younger persons and the mild cases in older ones. In this study, however, the average age in the mild cases was 31.2 years, in the moderate cases 36.6 years and in the severe cases 34.4 years. Forty-two (22

TABLE 1. *Age Incidence of Diabetes Mellitus and Transient Glycosuria.*

AGE	PRESENT AGE OF 208 DIABETIC MEN	AGE AT ONSET OF DIABETES IN 189 DIABETIC MEN	PRESENT AGE OF 126 MEN WITH TRANSIENT GLYCOSURIA	PRESENT AGE OF 1000 NONDIABETIC MEN
yr.	%	%	%	%
2-7		1		
8-16		4		
18-25	19	20	39	43
26-30	13	15	11	17
31-35	15	17	14	11
36-40	20	15	16	15
41-45	33	28	19	14
Average ages	34.4 yr.	33.0 yr.	30.9 yr.	27.5 yr.

per cent) of 189 diabetic men had a known duration of the disease for one to twenty-three years, and the average age at onset of diabetes was 33 years, or 1.4 years lower than the average present age of all the diabetic men.

Diabetes is generally regarded as occurring with special frequency in the older groups, especially between the ages of fifty and sixty. Probably the incidence in the older age groups is not so great as previously thought because many people have undoubtedly had diabetes for some years without knowledge of it. As a result, a cumulative effect of age is obtained in later years of life. This effect was particularly brought out in a study of the present age and the age of onset of diabetes in 42 men who had had the disease for one to twenty-three years, as illustrated in Table 2. If

TABLE 2. *Present Age and Age at Onset of the Disease in 42 Diabetic Men with a Known Duration of One to Twenty-Three Years.*

AGE	PRESENT AGE	AGE AT ONSET
yr.	%	%
2-7		5
8-16		17
18-25		29
26-30	34	19
31-35	14	21
36-40	21	7
41-44	17	2
Average ages	31.8 yr.	24.2 yr.

one notes the age at onset of the disease in this group, there is a preponderance of diabetes in the younger men and fewer cases in the oldest age groups. Yet if one studies their present ages, a marked contrast is observed.

Weight. One of the chief constitutional features in the onset of diabetes has been considered to be overweight. Consequently a study of the

weight was made in 196 cases of diabetes mellitus and 103 cases of transient glycosuria. These results are given in Table 3. In the diabetic men, the weights were studied according to the mild, moderate and severe cases, and since the results were approximately the same in the various types of cases, the weights are reported for diabetes in general. The average diabetic man weighed 158 pounds and was 34.4 years old, whereas the average man with transient glycosuria weighed 151 pounds and was 30.9 years old. The averages of 1000 consecutive selectees were 140 pounds and 27.5 years. Weights ranging from 12 pounds above to 12 pounds below the Army standard⁶ for height and age were called normal. When a

TABLE 3. *Weight in Diabetic Men, Men with Transient Glycosuria and Nondiabetic Men.*

WEIGHT ACCORDING TO HEIGHT AND AGE (ARMY STANDARD)	196 DIABETIC MEN	42 DIABETIC MEN WITH DISEASE OF 1 TO 23 YEARS' DURATION	103 MEN WITH TRANSIENT GLYCOSURIA	1000 NONDIABETIC MEN
	%	%	%	%
Underweight				
30-40 lb.	3	6	0	7
41-48 lb.	11	14	22	10
Normal weight	48	57	53	56
Overweight:				
15-34 lb.	16	19	12	20
35-54 lb.	9	5	5	8
55-70 lb.	8	0	7	3
80-134 lb.	5	5	1	1
Average weights	158 lb.	151 lb.	151 lb.	140 lb.

correction of 5 pounds is made for the greater age of seven years in the diabetic group, the excess weight over the control group is 13 pounds. After an adjustment of nine pounds is made for the greater height and age of the men with transient glycosuria, their excess weight is only 2 pounds. It is the few markedly obese diabetic men who increased so much the average weight of all the diabetic men.

Approximately 62 per cent of all the diabetic men, 75 per cent of those with transient glycosuria, and 68 per cent of the nondiabetic men were of either normal or subnormal weight. On the other hand, 38 per cent of the diabetic men, 25 per cent of those with transient glycosuria and 32 per cent of the nondiabetic men were 15 to 134 pounds above the standard. The weights of the men who had had diabetes for one to twenty three years were not significantly different from those of the control group.

Height. The heights of the men with diabetes mellitus and transient glycosuria ranged from 60 to 74 inches, as shown in Table 4. The average height of the diabetic men was 66.0 inches and of those with transient glycosuria 67.8 inches (In Joslin's male adult diabetic patients,⁷ the aver-

age height was 67.2 inches.) These compare with the control height of 66.4 inches based on the measurement of 1000 consecutive selectees. The diabetic men appeared of average normal height,

TABLE 4. *Heights in Diabetic Men, Men with Transient Glycosuria and Nondiabetic Men.*

HEIGHT	205 DIABETIC MEN	42 DIABETIC MEN WITH DISEASE OF 1 TO 23 YEARS' DURATION	122 MEN WITH TRANSIENT GLYCOSURIA	1000 NON- DIABETIC MEN
	%	%	%	%
60-63	19	16	10	10
64-66	34	26	33	33
67-68	27	31	24	26
69-71	19	23	28	26
72-74	1	4	5	5
Average heights	66.0 in.	66.7 in.	67.8 in.	66.4 in.

whereas those with transient glycosuria were 1.4 inches above the normal, a fact that appears significant. Most of the men with glycosuria were between 64 and 68 inches tall.

Blood pressure. The blood pressures were studied in all cases. Hypertension that was comparatively mild (over 150 systolic, 90 diastolic) occurred in 7 per cent of the diabetic men and in 5 per cent of those with transient glycosuria. The diastolic pressures ranged from 80 to 124, and the systolic from 160 to 194. The incidences of hypertension in the severe diabetic cases and those of transient glycosuria were somewhat less than those in the mild and moderate diabetic cases, as shown in Table 5. In the 42 men with diabetes

TABLE 5. *Incidence of Hypertension in Various Groups of Diabetic Men, Men with Transient Glycosuria and Nondiabetic Men.*

	207 DIABETIC MEN			126 MEN WITH TRANSIENT GLYCOSURIA	1000 NON- DIABETIC MEN
	107 MILD CASES	58 MODER- ATE CASES	42 SE- VERE CASES		
Incidence of hypertension	7.5%	7.0%	5.0%	5.0%	2.2%

of one to twenty-three years' duration only 1 had an increased blood pressure (170 systolic, 110 diastolic).

Pulmonary tuberculosis. Pulmonary tuberculosis has been considered in the past as a significant complication of diabetes.⁸ The opportunity seemed excellent to compare the routine x-ray findings of the chest in diabetic men and in those with transient glycosuria with those in nondiabetic persons. In 208 cases of diabetes not an active case of pulmonary tuberculosis was found, in contrast to the average incidence of pulmonary tuberculosis of 0.9 per cent found in a one-year

study of selectees.⁹ There was, however, one nodular or arrested case and 6 cases of healed primary tuberculosis, which is consistent with the average of 3 per cent primary tuberculosis found by x-ray in nondiabetic persons. In 126 cases with transient glycosuria there were 2 cases with minimal pulmonary tuberculosis and 1 with moderately advanced tuberculosis. Root¹⁰ believes that the susceptibility of diabetics to pulmonary tuberculosis depends largely on the control of the diabetes. However, in our group, which consisted chiefly of men with uncontrolled diabetes, there appeared to be the same amount of pulmonary tuberculosis in the persons with glycosuria as in all other volunteers and selectees examined.

Physical condition. In general the physical condition of all the diabetic men and of those with transient glycosuria did not differ from the control group except for the increase in the incidence of hypertension, and the slight increase in the average weight of the diabetic men. No other endocrine disturbances were noted. On the whole it is fair to say that the diabetes had no effect on the physical state of the 42 persons aged eighteen to forty-five who had had this disease for one to twenty-three years. As a matter of fact, they were essentially free of vascular disease and, as previously mentioned, only 1 had an elevated blood pressure.

Treatment. The diabetic men discovered on routine examination had had no particular previous treatment. Of the 42 men who knew that they had had diabetes mellitus for one to twenty-three years, 11 cases were moderate, 6 were mild, and 25 were severe. Therapy in 9 of the 17 mild and moderate cases consisted of diet only, whereas 4 received small doses of insulin, 3 followed no treatment and no record of treatment was made in 1 case. Of the 25 severe cases, 19 took some form of insulin. Twelve injected daily 26 to 100 units of protamine insulin, and 5 of these received in addition 12 to 40 units of regular insulin a day. Seven patients took regular insulin only in daily amounts of 30 to 83 units a day divided into one to three doses. Three followed a diet only and 1 followed no specific treatment. No record of treatment was made in 2 cases.

Family history of diabetes. The inheritance of diabetes has been pointed out by many writers. The family history of diabetes was studied in 126 cases of diabetes mellitus and in 77 cases of transient glycosuria. The familial incidence of diabetes in mild, moderate and severe diabetic cases was much the same. Of 126 diabetic persons interviewed, 41 (32 per cent) gave a family history of this disease, which had occurred in one to seven members of the family. There was a family

history of diabetes in 36 per cent of the diabetic men who had had the disease for one to twenty-three years, and in 30 per cent of those cases that were discovered on routine examination. Of the 77 men with transient glycosuria, 7 (9 per cent) gave a family history of diabetes, which had appeared in only one or two members of each family. In a control study, 2293 consecutive non-diabetic selectees were interviewed and only 119 persons (5.2 per cent) gave a family history of diabetes; this occurred in all cases in only one member of the family. An analysis of the diabetic relatives is given in Table 6.

The diabetic relatives of the 41 diabetic men with a family history of diabetes amounted to 68. Of these, 29 had a history of the disease in only one member of the family. In 12 diabetic cases the disease had existed in two to seven members of each family, with a total of 39 diabetic relatives,

TABLE 6 *Diabetic Relatives of Diabetic Men, Men with Transient Glycosuria and Nondiabetic Men.*

RELATION	41 DIABETIC MEN	7 MEN WITH TRANSIENT GLYCOSURIA	119 NONDIABETIC MEN
Grandparent	1	0	20
Mother	13	3	47
Father	13	3	46
Brother	12	1	2
Sister	12	0	1
Aunt	7	0	1
Uncle	7	1	1
Cousin	2	0	1
Total	68	9	119

as follows: 6 with two relatives each, 2 with three relatives each, 2 with four relatives each, 1 with six relatives, and 1 with 7 relatives. Of the 7 men with transient glycosuria, 5 gave a history of diabetes in one member of the family and 2 in two members of the family.

COMMUNITY STUDIES

Community desirability. The classification of the community desirability was based on the seven factors of medical care, educational and recreational facilities, crowded housing, social class, public works and welfare rate. The good communities, largely well-to-do residential areas, were superior in all these aspects; the poor communities, with low ratings in these factors, were poor, crowded tenement areas; and the medium classification included all the intermediate socioeconomic gradations of the middle class. The incidence of diabetes in relation to community desirability is shown in Table 7.

This study shows no significant variation in the prevalence of diabetes mellitus in selectees from communities of different socioeconomic levels. This lack of relation to socioeconomic background

is quite unexpected in view of the stress that has been placed on the influence of inactivity and increased diet among the upper classes, but is what

TABLE 7. *Prevalence of Diabetes Mellitus According to Socioeconomic Level of the Community*

TYPE OF COMMUNITY	NO. OF MEN EXAMINED	PERCENT MEN WITH DIABETES MELLITUS
Good	5 221	0.71
Medium	17 059	0.73
Poor	7 869	0.75

might well be expected in a disease of such hereditary nature.

Communities were also classified by welfare level, on the basis of the amount of welfare paid per capita, as given by Lambie.¹¹ The relation of diabetes mellitus to the welfare rate of the community from which the selectees come is shown in Table 8. This relation shows that there is little variation in its incidence at different community welfare levels. In contrast, the total rejection rate for all causes increased in the poorer communities and in those with higher welfare rates, as might be expected from poorer living conditions and medical care, which are so often concomitants of increased welfare.

Previous work on diabetes¹² has suggested that this finding would be different—that is, a decrease in diabetes in the communities with the highest welfare rates, because of greater privation, and an increase in diabetes in the upper classes because of excess food intake and sedentary occu-

TABLE 8. *Prevalence of Diabetes Mellitus According to Community Welfare Rate*

ANNUAL PER CAPITA WELFARE RATE	NO. OF MEN EXAMINED	PERCENT MEN WITH DIABETES MELLITUS
Less than \$20	4759	0.7
\$20-29	4919	0.5
\$30-39	8909	0.6
\$40 and over	3 24	0.8

pations. This, however, is not shown, since the communities with the highest welfare had 0.8 per cent of diabetes mellitus and the lowest bracket had 0.7 per cent.

Population density. Communities were grouped according to population per square mile, and their incidences of diabetes are shown in Table 9. The higher prevalence of diabetes in the communities with higher population density can hardly be explained by chance.

An increase of diabetes in urban areas has been recognized by Joslin,¹³ who explains it in several

ways: more sedentary living, a higher economic level with more abundant eating and a larger element of Jews in the population, with their high prevalence of diabetes. Previous findings indicating the failure of the community socioeconomic

TABLE 9. *Prevalence of Diabetes Mellitus According to Population Density.*

POPULATION PER SQUARE MILE	NO. OF MEN EXAMINED	MEN WITH DIABETES %
Under 1000	3928	0.4
1000-4999	7613	0.5
5000-9999	6778	0.8
10,000-19,999	7179	1.0
20,000 or over	5479	0.8

level to influence diabetic prevalence and the lack of relation to laborious occupations suggest that these factors cannot be considered in the interpretation of the increased prevalence of diabetes in increased population densities. The factor of nationality appears to be, in part at least, a satisfactory explanation for the high prevalence of diabetes in dense urban areas, for both Jews and Irish are concentrated in the urban high-density areas in sufficient number to elevate the prevalence to about 0.8 per cent for those areas from 0.4 per cent in the least populated regions. There may be other, as yet undetermined, factors relating to population density, but it will take much further investigation to demonstrate them.

Occupation. Occupation has been considered to be an important predisposing factor of diabetes mellitus, which has been thought to occur with much greater frequency in persons with sedentary occupations than in those with laborious occupations. Types of occupations were studied in 118 diabetic men and in 81 with transient glycosuria and compared with the occupations of 1400 consecutive selectees and volunteers.

Occupations were divided into three types, as follows: "white collar," light labor and heavy labor. The white-collar group included clerks, students and business and professional men. The light-labor group included factory and mill workers, taxi drivers, drivers of light delivery trucks, salesmen, pipe fitters, painters and electricians. The heavy-labor group included longshoremen, drivers of heavy trucks, shipyard welders, masons, plumbers, carpenters and farmers. The results are shown in Table 10.

It was most interesting to find that the percentages of diabetic men doing heavy labor, light labor and white-collar work were almost identical with those of the control group. The results with transient and renal glycosuria were also similar. These observations appear significant, and strong-

ly suggest that occupation in general is not a predisposing factor in the etiology of diabetes.

Those communities in which there was one predominant occupation were classified and the prevalence of diabetes considered as shown in Table 11. A great variation existed with shoe-manufacturing towns and urban commuters' areas having the greatest amount of diabetes. This again suggests that diabetes is as common in those engaged in manual labor as in those in sedentary occupations, for both the workers in the shoe

TABLE 10. *Occupation Classified According to Glycosuria of Various Types.*

	WHITE- COLLAR %	LIGHT LABOR %	HEAVY LABOR %
No glycosuria	24	63	13
Diabetes	24	64	12
Transient glycosuria	20	75	5
Renal glycosuria	27	68	5

towns and the urban commuters' areas were for the most part doing manual labor, although many were clerks and office workers. The low prevalence in farming and fishing communities is hard

TABLE 11. *Incidence of Diabetes in Communities with a Dominant Occupation.*

OCCUPATION	INCIDENCE OF DIABETES %
Leather and shoe manufacturing.....	1.3
Urban commuters	1.2
Suburban commuters	0.9
Textile workers	0.6
Farming	0.5
Fishing	0.4

to understand. It is partially explained by the almost complete absence of both Jewish and Irish elements from the population of these areas, and Joslin's explanation that these groups are engaged in the hardest type of manual labor may pertain although it does not coincide with our finding.

Nationality. The incidences of the nationalities of 128 persons with diabetes mellitus and 88 with transient glycosuria were compared with that of a control group of 7350 consecutive persons at this induction station. The results are shown in Table 12. The nationality was determined according to the birthplace of the parents of the men examined. For example, the nationality was called American when both parents were born in this-country. If a selectee was born in this country and his parents in Ireland, his nationality was called Irish. The Jewish persons were ordinarily Russian, Polish or Austrian.

The findings of the nationalities appeared of considerable interest. Of the men examined, 45

per cent were Americans, but they constituted only 33 per cent of the diabetic group and only 21 per cent of those with transient glycosuria. On the other hand, the non-American group in general showed a greater incidence of diabetes and a much greater incidence of transient glycosuria than did the control group.

It appears that the longer are the generations of nationalities in this country, the more the inci-

have gone into mixed communities. It has special value as presented here, not only because it confirms the study of nationality but also because it shows to just what extent nationality can affect a community, and hence helps to explain the

TABLE 12. *Incidence of Diabetes and Transient Glycosuria According to Nationality.*

NATIONALITY	CONTROL GROUP	DIABETIC GROUP	GROUP WITH TRANSIENT GLYCOSURIA
	%	%	%
American	45	33	21
Irish	11	18	21
Italian	10	7	11
Jewish	6	13	9
Portuguese	5	5	1
Canadian	9	5	3
Other nationalities*	14	19	34

*French, Greek, English, Polish, Scottish, Negro, German, Lithuanian, Armenian and Syrian.

dence of diabetes diminishes, at least to a certain point, because of the low incidence in those classed as Americans, who are of course originally of foreign extraction. The Jews and Irish were of particular interest. The Jews had more than twice as many in the diabetic group as in the control group. The Irish, who constituted 11 per cent of the control group, showed a marked increase to 18 per cent of the diabetic cases and 21 per cent of those with transient glycosuria. The marked increase in the per cent of transient glycosuria in the Irish may possibly be explained on the basis of chronic alcoholism, because Hyde,¹⁴ as well as Haggard and Jellinek,¹⁵ found a high incidence of chronic alcoholism in the Irish. The French, with only 0.1 per cent of the control group, made up 4.7 per cent and 7.4 per cent of the groups with diabetes and transient glycosurias, respectively. The French and Canadian groups may not be reliable because some of the French were probably from Canada. If the French and Canadians are considered as a whole, the incidence of these conditions is practically the same as the control group. The group of other nationalities showed a marked increase in the percentage of transient glycosuria.

Those communities wherein a major element of the population was of one nationality by extraction were considered by nationality, as shown in Table 13. This presents a different aspect of nationality than that presented by a consideration of nationality alone, for a minority of other nationalities exists in the community, and persons in a foreign community present more habits and customs of the nationality than do those who

TABLE 13. *Prevalence of Diabetes According to Predominant Community Nationality.*

NATIONALITY	NO. OF MEN EXAMINED	PER CENT WITH DIABETES
Jewish	1014	1.8
Irish	835	1.3
Canadian	302	0.66
Italian	1791	0.50
Portuguese	1706	0.35

correlation of the incidence of diabetes with population density or other social considerations.

SUMMARY

This paper presents certain clinical and socioeconomic studies on diabetes mellitus and transient glycosuria that occurred in 45,650 consecutive selectees and volunteers, aged eighteen to forty-five years, who appeared for final examination at the Boston Armed Forces Induction Station.

The incidence of glycosuria was found to be 367 cases, or 0.8 per cent of the men examined. The cases of glycosuria were divided into three groups with the number of cases as follows: 208 cases of diabetes mellitus; 126 cases of transient glycosuria and 33 cases of renal glycosuria. Of the 208 cases of diabetes, 107 were mild, 58 were moderate and 43 were severe.

The average present age of the diabetic men was 34.4 years and that of the men with transient glycosuria 30.9 years, as compared with the average age of 27.5 years of the nondiabetic group. The average age at onset of all the diabetic men was 1.4 years lower than their present age. The average present age of those with diabetes of one to twenty-three years' duration was 31.8 years, compared with the average age of 24.2 years at onset showing how a cumulative effect of age is produced as the diabetic men grow older.

The average weight of patients with diabetes and transient glycosuria was slightly higher than that of the control group. However, 62 per cent of the diabetic men and 75 per cent of those with transient glycosuria, as compared with 68 per cent of the nondiabetic men, were of either normal or subnormal weight according to Army standards. Except in a few cases, obesity did not appear to be an important factor in these cases. The average height of the diabetic men was the same as that of the control group.

The physical condition of the men with glycosuria did not differ from that of the nondiabetic

men, except that mild hypertension appeared in 7.0 per cent of the diabetic men and in 5.0 per cent of those with transient glycosuria, compared with 2.2 per cent in the control group. Pulmonary tuberculosis as determined from chest roentgenograms appeared with essentially the same frequency in the persons with glycosuria as in all the volunteers and selectees examined.

The inheritance of diabetes was of interest because family histories of diabetes were obtained in 32 per cent of the diabetic cases and in 9 per cent of those of transient glycosuria, as compared with 5.2 per cent of 2293 consecutive nondiabetic selectees. The number of diabetic relatives per family of each diabetic man was appreciably greater than that of the nondiabetic men.

Occupation did not appear to be a predisposing factor in the etiology of glycosuria, since the percentages of the men with glycosuria doing hard labor, light labor and white-collar work were almost the same as that in the control group.

Community studies of diabetes showed that the prevalence of diabetes was the same in communities of good, medium and poor socioeconomic levels. The relation of the prevalence of diabetes to community welfare rates showed little variation at the different community levels. In contrast, previous studies of diabetes have suggested that there is a decreased incidence in communities with the highest welfare rate, owing to privation. There was a higher prevalence of diabetes in communities with a high population density. Nationality seems to be, in part at least, an explanation for this phenomenon.

The nationalities, as based on the birthplace of the parents of the selectees, were studied. The incidence of diabetes and transient glycosuria was lower in the American group and higher in the non-American group, as compared with the incidence of the nationalities in the control group. The incidences of diabetes in the Jews and the Irish were outstanding.

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CURRENT CONSIDERATIONS OF THE ARMY ANESTHESIOLOGIST*

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MILITARY campaigns necessitate medical preparedness. The expanded Army today is serviced by an enlarged and one of the most competent medical departments ever organized. All pertinent specialties are represented, and key personnel are virtually hand-picked. Notwithstanding a roster of 35,394 medical officers on active duty,¹ the proportion of officer anesthetists to other medical specialists is still surprisingly low. The need for such personnel has arisen not only from the greater number of hospital installations but particularly from the growing appreciation of the services such officers can render. To many, this demand, as well as the recognition of anesthesiology by the Army, has presented a challenge met only by requests for active duty in the armed forces. Thus far, two hundred and seventy-eight members of the American Society of Anesthetists, thirty-nine of whom are diplomates of the Board of Anesthesiology, are serving in the Army as anesthetists.² The total number is still short of the quota desired, and thus it may be expected that many more of our civilian confreres will join our ranks. To facilitate their early orientation with respect to military anesthesia as well as to elucidate a few of their professional duties to civilian surgeons, internists and general practitioners, some of the current considerations of the Army anesthesiologist will be presented. These may be logically grouped as those of basic and those of specific nature.

BASIC CONSIDERATIONS

Scope of Anesthesia

The present-day military anesthetist is no longer the glorified medical technician of World War I, nor is he a superman of the present conflict. He is simply one link in the chain of command of a surgical installation. However, his sound training in the fundamental principles of physiology, pharmacology, anatomy and so forth and his thorough appreciation of their clinical application have made him indispensable to surgeons. His anesthetic duties are clear cut and not unlike those of his civilian colleagues. According to the present scope of anesthesia per se (Table 1), his primary obligations to his patient and surgeons concern adequate preoperative preparation; relief of pain;

muscular relaxation, prophylaxis and therapy for adverse cardiorespiratory derangements during surgery; and prompt and effective postoperative care to prevent or minimize complications of circulation or respiration. In addition, he may be

TABLE 1. *Present-Day Scope of Anesthesia.*

SURGERY	MEDICINE
Preoperative	Diagnostic
Diagnosis	Peripheral vascular disease
Premedication	Hypertension
Operative	Therapeutic
Analgesia	Asthma
Relaxation	Angina
Prophylaxis	Intractable pain (cancer)
Therapy	Resuscitation (gas and drug poisonings)
Postoperative	Suicida
Complications	
Therapy	

of some aid to the internist with the use of diagnostic or therapeutic blocks in treating peripheral vascular disease, the intractable pain of cancer, angina pectoris or status asthmaticus, or with the help of resuscitative measures in combating gas or drug poisonings. These duties constitute the minimal requirements of a competent anesthetist, military or civilian.

Orientation of Anesthetist

Notwithstanding their successful professional background, civilian anesthetists entering military service go through a period of orientation. Quite apart from adapting themselves to Army regulations, they become impressed early with the fact that favorite agents and pet technics are not always popular or possible to employ. Such a practice is not conducive to good anesthesia, even in civilian life, where anesthetic management of patients should also be individualized and not routine. Orientation to the use of many accepted anesthetic agents and technics is simple and rapid with competent anesthetists but difficult and uncertain with others. The Army supplies a variety of agents and equipment—a policy that meets not only the demands of the physical status of all patients but also the necessities of surgeons. Furthermore, such a plan may better facilitate the activities of an anesthetist in a mobile surgical hospital whose armamentarium and supplies are affected by combat situations. Accordingly, many anesthetists have had to relearn their technics of open-drop ether and chloroform as well as the advantages and limitations of both. Others have had to review their procedures of spinal and intravenous

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anesthesia and human anatomy to perform block anesthesia more successfully. In this phase of orientation, refresher courses³ have been helpful to many.

Organization of Section

Officer anesthetists, assigned to hospital units or surgical teams, after their orientation and basic military training are immediately confronted with the problem of organizing their section. The scope of this problem depends on the type, size and location of the unit as well as on its general functions. In named general and station hospitals, which also serve as training centers, the complement of the Section on Anesthesia and Operating Pavilion may be as large as twenty persons, consisting of two officers, four nurses and fourteen enlisted men. In small units, such as surgical teams, there may be only one officer anesthetist and an enlisted man trained by him. The anesthetist supervises the activity of his personnel, making them available for surgery on a twenty-four-hour basis. This includes not only anesthesia but also the preparation of the entire operating pavilion, the latter duty being totally foreign to the average civilian anesthetist. He requisitions bi-weekly expendable supplies, such as anesthetic agents, gauze, antiseptic solutions and ligatures, and is responsible for the care, repair and availability of all anesthetic equipment and surgical instruments. Finally, to promote the prime function of his section in scheduling and facilitating surgical procedures, he must incorporate in the local hospital regulations certain definite, clear-cut and fundamental policies referable to the interrelations of his section with the surgical service as well as with medical, dental and laboratory services. The regulations should include comment on the matter of scheduling operations and preparing and premedicating patients, transporting them to and from the operating pavilion and prescribing the first postoperative treatment. In this general plan of organization, attention must be given to Army regulations and to the many helpful suggestions of the commanding officer and chief of the surgical service.

SPECIFIC CONSIDERATIONS

General Functions of Section Chief

Once the period of organization has ended and the Section on Anesthesia and Operating Pavilion is performing satisfactorily, the anesthetist or section chief can assume additional duties. These have been emphasized elsewhere.⁴ His activities, briefly, can be of an administrative, professional or miscellaneous nature. Those of professional character may include not only the scheduling of all

surgical procedures and the administration and supervision of anesthesia, but also the sterilization and autoclaving of equipment and laundry of all wards of the hospital as well as of the operating pavilion, the administration of plasma and whole blood and, finally, the centralization and supervision of inhalation therapy. It can readily be seen that the responsibilities of the military anesthetist are admittedly great and far more diverse than those of his civilian colleagues.

Records

The tabulation and maintenance of records are prerequisites of successful administration. The section chief of anesthesia has his share of the paper work to take care of. Aside from records referable to property accountability and requisition of expendable items, there are those pertaining to surgical procedures, anesthesia, pathology specimens and so forth. A composite record in book form of all surgical and anesthetic procedures may be authorized by the chief of the surgical service for future reference or compilation. Standard Form 55-0-1 is necessary for all operative patients, and includes data of the preoperative status of the patient and his progress during anesthesia. These may be of inestimable value to a patient being considered for limited duty, discharge or retirement. Wangeman⁵ has suggested the use of a modified Hollerith punch card to compile surgical and anesthetic data in the Army for statistical studies.

Instruction of Personnel

One of the most important duties of the chief of Section on Anesthesia and Operating Pavilion concerns the instruction of his personnel. This applies to his officers, nurses and enlisted men. It is vitally necessary to ensure optimum efficiency of the section at all times, particularly in view of the fact that initially many of the personnel are inadequately trained for the functions they are to perform or, when trained, may be replaced by newcomers, owing to illness, combat injury or reassignment as a nucleus for new hospital units. Instruction is essentially of two types: training of surgical technicians and training of anesthetists. With the help and supervision of an experienced responsible and competent chief operating-room nurse, enlisted men of the medical detachment can be instructed satisfactorily within three months in the duties of scrub or circulating nurses and sterilizing-and-autoclave-room attendants. It has been particularly gratifying to see the proficiency attained and enthusiasm shown in these duties by enlisted men who have had no more than high school or general college training.

Training in anesthesia has been conducted by the chief anesthetist in almost every hospital unit owing to shortage of such personnel. The type and duration of the course have varied at different posts depending on the instructor, his teaching ability and the background of his students. Through the kind suggestions and wholehearted co-operation of Colonel S. Jay Turnbull, the first organized course in anesthesia in the history of the Army, consisting of a series of lectures, demonstrations and practical supervision in the operating room, was given at Tilton General Hospital in July, 1941.⁹ A year later the School of Anesthesia was officially authorized by the War Department, and several courses have since been given. Such training was designed to meet military needs. It was intensive and all-inclusive for the officers, but concerned only open-drop technic for the enlisted men. To conserve nurse personnel, and particularly to take advantage of the extensive laboratory background of many of the enlisted men, who could also be assigned to arduous duties in the operating pavilion when not administering anesthesia, enlisted men were preferred to nurses as students.

For medical officers, emphasis was given to inhalation, spinal, intravenous and block anesthesia with respect to the agents and equipment supplied by the Army. Fundamental principles and their clinical application were studied with agents such as ether, ethyl chloride, chloroform, nitrous oxide, procaine, Metycaine, and Pentothal Sodium, administered by technics suitable for mobile or fixed hospitals. Other agents, such as Vinethene, cyclopropane and nupercaine, and procedures such as continuous spinal or caudal anesthesia were demonstrated to indicate their particular usefulness for definitive surgery at fixed general hospitals. In addition, special attention was given to instruction in endotracheal technics, methods of resuscitation, inhalation technics and fluid or shock therapy. No effort was spared in the intimate supervision of practical training and of adaptation to military necessities.

Anesthetic Management. at Various Medical Echelons

Considerations of anesthetic management constitute some of the most practical and significant problems the military anesthetist has to contend with. They are of prime importance to him, for therein lies his usefulness to his unit. To appreciate their magnitude fully, in contrast to the relatively complacent routine of the civilian anesthesiologist, some pertinent factors concerned will be mentioned.

Type of injury. Injuries may be those of the thorax, abdomen, extremities, central nervous

system or maxillofacial region, or any combination of these. They require different technics and agents, and the choice of these by the anesthetist may play a significant part in the surgeon's program.

Severity of injury. Injuries should be classified and separated according to their major or minor character to expedite prompt and effective treatment of the more serious casualties.

Accompanying condition of patient. Major surgery may often be handicapped by delays in diagnosing and providing early treatment for patients showing asphyxia, variable degrees of peripheral vascular collapse, physical exhaustion, inanition, and exposure to extremes of temperature, sandstorms or snowstorms or tropical diseases.

Time interval between injury, diagnosis and treatment. This factor is admittedly of more importance to the surgeon than to the anesthetist, although its appreciation by the latter will favor a satisfactory anesthetic management.

Number of cases. Medical units, as in World War I, will either be in a state of readiness or be deluged with mass casualties. This latter situation will profoundly affect the anesthetic management in that individual considerations will be outweighed by those of the entire group.

Weapons or methods used in producing casualties. Patients exposed to gas attacks or suffering from blood loss may require resuscitation or shock therapy. Others showing tissue trauma will need surgery. A knowledge of the weapon causing the injury will aid the anesthetist in his plan of action.

Medical service available. Of all factors enumerated, the availability of medical service in the Army is of the greatest interest to the patient, the surgeon and the anesthetist. This problem has been fully appreciated, and after years of experience, intensive study and competent organization, the Medical Corps has developed the highest degree of efficiency in its history. Its functions of first aid on the battlefield, emergency treatment, evacuation and hospitalization of patients for definitive treatment are now being effectively carried out notwithstanding the complexities and difficulties of fluid and far-flung fronts. To the anesthetist, among others, it is imperative to understand the general plan of organization the anesthetic armamentarium available at the various medical echelons and the probable anesthetic management at these locations.

The medical service of the Army is divided into five echelons, the first three of which are mobile and attached to tactical troops, and the last two of which are stationary or relatively fixed⁷ (Table 2). The unit medical services, located some three

medical officers are assigned to all five echelons, the anesthesiologist is first found in installations of the Army medical service along with surgical

TABLE 3. *Anesthetic Armamentarium in the Medical Services of the Army.*

TABLE 2. *Outline of Medical Services of the Army.*

MOBILE:
Unit — battalion aid stations
Divisional: Collecting and clearing stations Surgical hospitals (Army supported)
Army: 1st echelon — battalion aid stations (as above) 2nd echelon — collecting and cleaning stations (as above) 3rd echelon — surgical (as above) and evacuation hospitals 4th echelon — numbered general and station hospitals (as below) 5th echelon — named general and station hospitals (as below)
FIXED:
Theater of operations (territorial commands): Numbered general hospitals Numbered station hospitals
Zone of interior (Surgeon General): Named general hospitals Named station hospitals

hundred to eight hundred yards behind forward-moving infantry, receive wounded by litter and provide emergency treatment, given in addition to the first aid administered on the battlefield. The divisional medical services, some twelve hundred to thirty-five hundred yards back, continue emergency treatment and sort out patients to be retained or to be evacuated to the rear. Several miles back may be found installations of the Army medical service, where surgeons, anesthetists and other medical specialists may be found. All types of emergency surgery may hence be performed. Some of these installations, such as surgical teams, may be sent forward in divisional areas for duty to facilitate early and prompt treatment. Thus the surgeons and the anesthetists are brought to the patient. This procedure obviates the necessity of transporting the seriously wounded, who can ill afford added physical strain. Units of the theater of operations may be one hundred to five hundred miles from combat areas, and those in the zone of interior are located in this country. In both these echelons, medical specialists are available to perform elective or definitive surgery or both. In the named general hospitals, both the personnel and the equipment are not unlike those found in leading hospitals of this country.

All types of medical services are adequately equipped with an anesthetic armamentarium for the duties that they are expected to carry out. No suffering need be experienced, for relief of pain may be provided anywhere from the battlefield to home stations. Table 3 briefly summarizes the type of anesthetic agents and equipment that may be found at the various medical services. Whereas

MEDICAL SERVICES	ASSIGNED ANESTHETIST	ANESTHETIC ARMAMENTARIUM	
		AGENTS	EQUIPMENT
Unit	No	Ether Ethyl chloride Morphine sulfate Atropine sulfate Procaine Ephedrine Barbiturates	Yankauer mask
Divisional	No	Same, except for Army-supported surgical hospitals (see below)	
Army	Yes	Same as above plus: Nitrous oxide Oxygen in tanks Chloroform Pentothal sodium Metycaine	Same as above plus Pharyngeal airways Laryngoscopes Endotracheal tubes Apparatus for closed-system anesthesia Modified suction apparatus Oxygen masks Needles and syringes for spinal and block anesthesia
Theater of operations	Yes	Same as above plus: Cyclopropane in some theaters	Same as above plus Other equipment depending on theater
Zone of interior	Yes	Same as above plus: Avertin Certain nonstandard items, such as Vinylene, Nupercaine, Pontocaine and so forth	Same as above plus Suction apparatus Iron lung Oxygen masks and tents Nonstandard items such as continuous spinal anesthesia equipment and so forth

specialists. No equipment is lacking to provide the patient with safe, modern anesthesia.

Owing to dynamic elements of combat, it is not possible to carry out in forward areas the anesthetic program that may be desired any more than it is possible to do ideal surgery in the battlefield. Safe and adequate anesthetic management, however, can be provided for the surgery that can and must be done. In Table 4, it can be noted that relief of pain and muscular relaxation or both can be accomplished even in the unit medical services for emergency surgical procedures, such as débridement, control of active external bleeding, application of painful splints and bandages, and the severing of a mangled limb. For major and more specialized surgery, done from the Army medical service to the rear, a

choice of agents and technics may be had depending on the patient, the surgeon and the surgery contemplated. Anything from simple premedication and local infiltration to closed-system en-

TABLE 4. *Anesthetic Management in the Medical Services.*

MEDICAL SERVICE	TYPE OF SURGERY	ANESTHETIC MANAGEMENT
Unit	Emergency	Emergency treatment: asphyxia, shock, relief of pain and anesthesia for minor surgery. Local infiltration or open drop technics
Divisional	Emergency	Essentially same on larger scale, except for Army supported units (see below)
Army	Emergency (general and specialized)	Local infiltration or block anesthesia Inhalation anesthesia—open-drop, closed-system and endotracheal technics Intravenous anesthesia Spinal anesthesia
Theater of operations	Elective and emergency	Same as above, except for advantages of better condition of patient and more complete anesthetic armamentarium
Zone of interior	Elective and definitive	Same as above plus nonstandard agents and equipment similar to those in leading hospitals of country

doctracheal anesthesia may be performed. Anesthetic management may thus be individualized and not routine. The same principles concerning contraindications of agents and technics, practiced by the civilian anesthetist will be adhered to at Army installations. The Army casualty will thus receive as good anesthetic management as does the civilian patient, if not better.

DISCUSSION

The history of the military anesthetist in this country has closely paralleled the rapid development of anesthesiology. It can conveniently be divided into three distinct eras: prior to 1863, when anesthetists were practically unheard of in civilian and military hospitals; from 1863 to 1919, when the few anesthetic agents and technics known to anesthetists were employed in military installations⁸; and from 1919 to 1943, during which time anesthesiology became established and accepted as a medical specialty by the American Medical Association,⁹ and during which the Army designated the Section on Anesthesia and Operating Pavilion in station and general hospitals¹⁰ and authorized the status of an officer for an anesthetist in charge of such a section. The progress of the civilian anesthetist in the latter interval has been tremendous and far-reaching in its influence on military anesthesia. Aside from the introduction of new agents such as cyclopropane, Vinethene, Pentothal Sodium, avertin, Metycaine and Pontocaine and procedures such as the Waters¹¹ closed carbon-

dioxide absorption system of anesthesia, endotracheal and endobronchial technics, intravenous anesthesia (Lundy¹²), regional anesthesia (Labat¹³) and continuous spinal¹⁴ and caudal¹⁵ anesthesia, there developed a keen and thorough appreciation of the fundamental physiologic, pharmacologic and anatomic principles underlying all anesthetic management. The present-day military anesthetist has kept abreast of the progress of his civilian confreres and is infinitely better prepared to function in his surgical unit than were his predecessors.

Notwithstanding the fact that the Army anesthesiologist is indispensable in military hospitals, there is still a shortage of such personnel on active duty. Some³ have believed that there is an inadequate number of trained civilian anesthetists. Perhaps one of the reasons to account for the shortage of such trained men was the former lack of an organized training program for medical students, interns and residents. This, however, has been overcome by teaching outlines and laboratory and clinical investigations already published and available to all who are interested. It is more probable, however, that because anesthesiology per se is a relatively new medical specialty, some hospitals and medical schools have been reluctant to accept it as such. If true, this is a sad commentary on medical leadership, for anesthesia is a true American contribution to medicine. This situation seems to present a professional if not a patriotic challenge to those institutions still lacking modern organized departments of anesthesiology. With such departments in hospitals and medical institutions, competent anesthesiologists could be trained in large numbers for urgent military and civilian needs, and some of the current considerations of the Army anesthesiologist would be greatly minimized. His role in providing the safest and most modern anesthesia for military casualties would be even more significant than it now is.

SUMMARY

The military anesthesiologist has contributed significantly to the prompt and efficient service of the medical department of the Army. Whereas his current considerations have been many and quite diverse from those of his civilian confreres, he has materially aided the function of his surgical unit. Some of his problems and functions have been briefly summarized.

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MEDICAL PROGRESS

THE GRAVE INFECTIONS OF THE HAND

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LYMPHANGITIS, acute suppurative tenosynovitis and deep fascial-space abscess have been well named the grave infections of the hand. Any review of these conditions must be considered on an anatomic, clinical and therapeutic basis.

LYMPHANGITIS

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There are two types of lymphangitis, deep and superficial. Deep lymphangitis involves the deep lymphatic vessels, which are found in the deep tissues in association with the deep blood vessels. Superficial lymphangitis involves the superficial vessels, which arise in the skin. The collecting trunks of superficial lymphatics run in the subcuticular tissue. A knowledge of the anatomy of

the lymphatics is basic for the proper understanding of the clinical aspects and treatment of lymphangitis.

The deep lymphatics follow the brachial artery and its chief branches, usually with two lymphatic trunks for each artery. The deep lymphatics of the upper extremity may be divided into radial, ulnar, anterior interosseous, posterior interosseous and humeral. The radial trunks drain lymph from the part supplied by the deep volar arch and the superficial palmar branch of the radial artery. They ascend the forearm as far as the bend of the elbow. The ulnar trunks drain lymph from the part supplied by the superficial volar arch and the deep and dorsal branch is the ulnar artery. The anterior interosseous and posterior interosseous lymphatics follow the arteries of the same names. The humeral trunks are two to three in number. They run by the side of the brachial artery and terminate in the humeral chain of axillary lymph nodes.

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the external surface. The majority of collecting vessels terminate in the axilla in the humeral chain of axillary nodes. Two or three of the most internal end in the epitrochlear lymph node. The efferent vessels of this node perforate the deep fascia in the middle of the arm and end in the deep vessels. When this gland is absent, the internal collecting vessels may perforate the fascia at the same point to reach the deep absorbing vessels. The most external trunk separates itself from the other collecting vessels in the region of the humeral insertion of the deltoid and ascends in the deltopectoral groove, where it may have one or several nodes. This trunk usually passes into a subclavian node, placed at the spot where the cephalic joins the axillary vein. Mascagni says that it may pass above the clavicle and empty into the supraclavicular node. Grossman states that this latter arrangement occurs in 38 per cent. of cases.

Lymphangitis was recognized in the earliest stages of surgery. Kanavel,³ however, reiterates the importance of differentiating lymphangitis from other grave infections of the hand, and stresses the need to distinguish deep from superficial lymphangitis. With deep lymphangitis there is usually a rapid increase of swelling of the whole hand and forearm, with some red lines running up the arm. Superficial lymphangitis usually lacks the rapid and great swelling of the entire hand and forearm. There is generally a history of abrasion of the hand. Red streaks are found extending up the arm. Kanavel emphasizes that with lymphangitis there is an absence of pain on hyperextending the finger and thumb, absence of tenderness over the tendon sheaths, voluntary movement of the fingers without pain, absence of bulging of the palm and absence of tenderness over the midpalmar and thenar spaces.

Until seven years ago, therapeutics in lymphangitis was based on the surgical principles of general rest, local rest, elevation of the part to facilitate lymphatic and venous drainage, local heat, proper diet, elimination and sedation. The specific treatment of lymphangitis dates from 1936, when Protosil, synthesized by Mietzsch and Klarer,⁴ proved by Domagk⁵ to be effective against the hemolytic streptococcus in mice, was shown by Colebrook and Kenny⁶ in their work on puerperal sepsis to be a potent chemotherapeutic agent in man.

Sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine have been used for lymphangitis. Many surgeons prefer sulfadiazine. When used in the proper dosage—4 gm. initially, 1 gr. every four hours for the first twenty-four hours and 1 gr. every six hours until the temperature remains normal for twenty-four hours—a blood level of

7 to 10 mg. per 100 cc is reached within six to eight hours, and is easily maintained. This blood concentration is adequate for bacteriostasis of the hemolytic streptococcus and *Staphylococcus aureus*, the organisms commonly found in lymphangitis. Clinically, sulfadiazine has the added advantage of being only slightly toxic.

Local measures designed to wall off and overcome the infection, together with procedures designed to support the system and increase its resisting power and to eliminate toxins, are necessary. In cases of lymphangitis until localization is present, warm moist dressings should be used and hospitalization should be insisted on, with local and generalized rest, together with cathartics, maximum fluid intake and sedatives.

Warm moist boric acid dressings are used locally. Such applications owe their value to the hyperemia caused by the moist heat rather than to the drug, although there is some evidence that the latter's chemical action is of value. The arm is placed on a sterile towel, and sterile dressings wet with a warm saturated solution of boric acid are applied. The dressings are covered with rubber sheeting and the rubber sheeting is enveloped in towels. Two perforated rubber tubes are inserted in the gauze pack, through which warm boric solution may be introduced every two hours. The heat is maintained by the use of hot-water bottles. In severe cases the dressings are applied to cover the entire arm and shoulder. The dressings should always be larger than the area involved in the infection.

Hospitalization and local and systemic rest should be insisted on, especially in severe infections. Immobilization is necessary because every movement of muscles of the fingers, hand, forearm and arm favors lymphatic circulation and dissemination of infection. The hand and arm should be elevated on pillows to provide for proper lymphatic drainage.

Incisions for lymphangitis should never be made except in the presence of abscess formation. Such incisions open new lymphatics for infection and fail to reach bacteria that have already entered the lymphatic stream.

Seriously ill patients should be given much fluid and small amounts of easily digested food. Large amounts of water or fluid by mouth are necessary. Fluids are of great value in diluting and eliminating toxins. Occasionally, intravenous saline and intravenous glucose solutions and blood transfusions are indicated.

The complications of lymphangitis are subcuticular abscess, lymph-node abscess, subpectoral abscess, suppurative tenosynovitis, subclavicular and shoulder abscess, septicemia and pyemia, and chronic or repeated infections.

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MEDICAL PROGRESS

THE GRAVE INFECTIONS OF THE HAND

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bloodless field is obtained by constricting the arm with a blood-pressure cuff inflated to 250 mm. The arm is elevated for one minute as soon as the patient is relaxed, and the blood-pressure cuff is inflated while the arm is still elevated. The arm

angers the vessels and nerves and may lead to herniation of the tendons.

Recently, Auchincloss¹⁰ has suggested the use of a truncated flap incision including all tissue down to the tendon sheath. In this incision, the distal

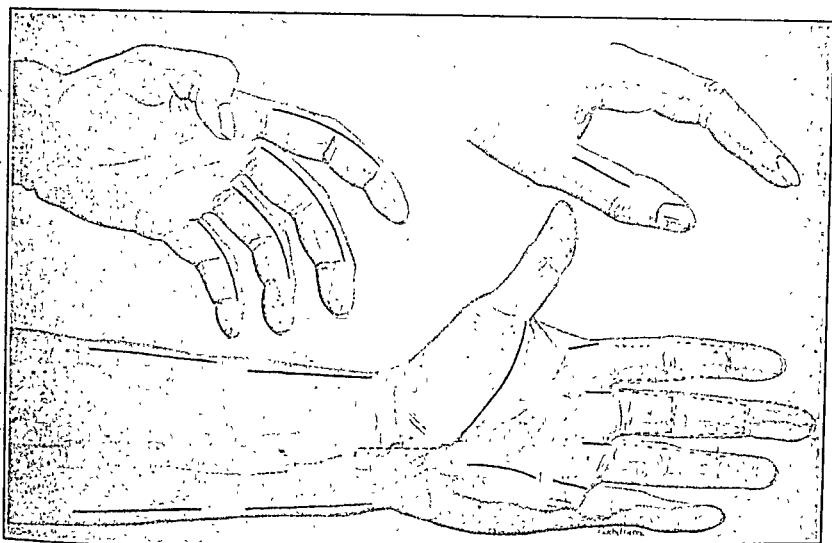


FIGURE 1. Incisions for Draining Infected Tendon Sheaths, Radial and Ulnar Bursas, Spaces in Wrist and Forearm. (Reproduced by permission of Surgery, Gynecology and Obstetrics.¹⁴)

The dotted lines represent rarely used incisions.

is then lowered, and a bloodless field can be maintained until the operation is completed. Only by good visualization can injuries to blood vessels and nerves be avoided, recognition of the site and extent of involvement be made, and adequate incisions with minimum injury be performed.

Surgically, Helferich,¹⁷ over fifty years ago, showed the need for an adequate incision of the involved sheath. Incisions should drain every pocket of pus. Until about 1930, it was common to make interrupted incisions over the medial and lateral aspects of the proximal and middle phalanges. These incisions have been discarded because drainage was incomplete, secondary incisions were required in too many cases, and the incidence of tendon slough was too great. It was also common to make medial or lateral incisions from the base of the distal phalanx to the level of the proximal volar digital crease, anterior to the digital vessels and nerves. These incisions are condemned because they necessitate cutting across the volar digital crease, and this procedure en-

ends is cut along the flexion crease. The medial and lateral parts of the flap are cut obliquely downward, the digital vessels and nerves being avoided, and the incision is extended nearly to the next proximal crease. The incision has been made over the proximal and middle closed spaces. Rubber tissue and thread have been used for post-operative drainage. It affords excellent exposure of the sheath, but the subsequent sloughing of tendons is often great, and the exposure of the tendon may be too extensive. Also, a rolling backward and sloughing of some of the distal part of the flap sometimes occurs, which delays healing.

Some knowledge of the underlying anatomy is basic for correct surgical treatment. The proper digital arteries are slightly posterior to the digital nerves, and are found at the level of the anterior third of the medial and lateral aspects of the fingers.

Auchincloss has shown that the digital arteries give off branches that form an anastomotic

arch of blood vessels in the anterior subtendinous space. This arch gives off vessels to supply the bone, the synovial membrane of the joint and the tendon sheath, and the tendon itself. The tendon receives its branches through the mesotendon or so-called "ligamenta brevis."

In my experience,¹¹ the lateral incision has proved of the greatest value. It extends from the distal crease to the proximal volar crease (Fig. 1). The incision is posterior to the lateral extensions of the volar transverse creases and posterior to the digital vessels and nerves. The only objection to it is that it involves cutting the branch from the digital artery that makes up part of the anastomotic arch of blood vessels in the anterior subtendinous space, from which the mesotendon is supplied. This small cut branch, however, is not an end artery, and anastomotic circulation from the other side appears to be adequate to nourish the tendon sheath and tendon. In almost all cases of septic tenosynovitis of the flexor tendons of the index, middle and ring fingers it is necessary to drain the palmar portion of the tendon sheath. This is accomplished by a longitudinal incision from the base of the proximal digital crease, which is carried about 2 cm. proximally into the palm. The incision is begun on the same side of the digital crease as the digital incision.

In the surgical treatment of infections of the little finger tendon sheath and the palmar portion of the ulnar bursa I¹⁴ use the following steps. A longitudinal incision is made over the lateral aspect of the little finger, posterior to the digital vessels and nerves and to the lateral extensions of the volar digital creases (Fig. 1). The palmar prolongation of the tendon sheath is drained by making an incision 2 cm. long from the center of the volar aspect of the proximal digital crease into the palm. The palmar portion of the ulnar bursa is drained by an incision extending from a point just proximal to the distal transverse crease in the palm to about the apex of the triangle in the base of the palm. The incision is made over the lateral edge of the hypothenar eminence. The digital branches of the ulnar nerve about 2 cm. proximal to the metacarpophalangeal joint, the anastomotic branch of the ulnar nerve to the median nerve and the ulnar artery about 1.5 cm. distal to the distal edge of the volar carpal ligament must be identified and medially retracted.

In the surgical treatment of infections of the thumb, a position of abduction of the thumb should be assumed to obviate anatomic distortion, particularly of nerves. I¹⁴ use a longitudinal incision from the base of the distal phalanx to the base of the thumb on the ulnar side (Fig. 1). The palmar incision is a separate one that starts at

about the middle of the proximal volar crease, just below the center of the volar aspect of the thumb. The incision is carried over the medial aspect of the thenar eminence, about two thirds of the distance to its base. The sensory and motor branches of the median nerve must be identified and retracted. At about the middle of the first metacarpal bone, a branch of the median nerve divides to send sensory branches to the medial and lateral aspects of the thumb. The important motor nerves to the opponens pollicis, abductor pollicis brevis and lateral portion of the flexor pollicis brevis, which rotate the thumb, arise from the median nerve, usually about 1.5 cm. proximal to the digital branches. The portion of the radial bursa proximal to where the nerves to the thenar muscles are found is not drained unless the volar carpal ligament is cut. The distal three fourths of the volar carpal ligament was cut in 2 cases in the series, not to expose the radial bursa but to avoid injury to the median nerve and flexor tendons. Incisions through the entire volar carpal ligament, as suggested by some surgeons should not be made because of exposure of the tendons and their prolapse.

Auchincloss¹⁰ stressed the fact that accumulations of pus in the radial and ulnar bursas in the wrist may rupture into the space bounded posteriorly by the pronator quadratus muscle and anteriorly by the flexor digitorum profundus and flexor pollicis longus tendons. From the wrist pus spreads up the forearm into the space bounded anteriorly by the flexor digitorum sublimis and posteriorly by the flexor digitorum profundus and flexor pollicis longus.

Various anterior, medial and lateral incisions have been described, but any incision into these spaces must be made with due regard for the underlying vessels and nerves. If both the ulnar and radial bursas are involved, or if pus has ruptured into the pronator quadratus space in the wrist, an incision on the ulnar side of the wrist may be adequate. I¹⁴ prefer an incision 6 cm. long over the anterior surface of the ulnar about 2 cm. above the styloid of the ulnar (Fig. 1). The approach is behind the flexor carpi ulnaris muscle and ulnar vessels. When the deep fascia is incised, the bulging ulnar bursa may be seen in the wound.

If the radial bursa alone is involved, an incision over the radial side of the wrist is made. A 6-cm. incision is made over the volar lateral aspect of the radius, as close to the bone as possible and posterior to the radial artery. When the deep fascia is incised, the bulging radial bursa may be seen in the wound.

Most infections from the wrist tend to spread up the ulnar side of the forearm, where most of the flexors are found. With infections of the intermuscular space of the forearm, a 6 cm. incision is made between the flexor carpi ulnaris and the ulnar margin of the flexor digitorum sublimis. The ulnar margin of the flexor digitorum sublimis is retracted laterally, and the space between it and the flexor digitorum profundus is entered by blunt dissection toward the latter. Great care should be taken not to injure the ulnar nerves and vessels that are adherent to the undersurface of the flexor digitorum sublimis.

An incision over the ulnar surface of the forearm, together with the wrist incisions, is usually adequate. With extensive accumulations of pus, however, an incision is made over the radial side of the forearm. The incision is about 6 cm. long at the middle third of the forearm and is made along the outer edge of the flexor carpi radialis. At this point, the lateral edge of the flexor digitorum sublimis muscle can be identified and retracted inward and the space entered by blunt dissection. The approach is internal to the radial artery.

Postoperatively, the infected hand is elevated on a pillow at all times to facilitate venous and lymphatic drainage. During the stage of acute infection, the hand and wrist are immobilized in an aluminum splint in the so called "position of function." If treatment is prolonged, this position favors early and satisfactory use and provides fixation in a useful position if disability ensues. The fingers are semiflexed, the wrist is dorsiflexed, the hand is extended in the cocked-up position, and the thumb is abducted and rotated so that its flexor surface is opposite that of the index finger. With the fingers and hand in the position of function, even though tendons may be lost or ankylosis ensues, a fair degree of function results. It is strongly advised to permit no motion until infection is controlled. With a sloughed tendon, however, in the absence of osteomyelitis or septic arthritis, the joints may be manipulated to prevent adhesions and to permit future tendon grafting. Warm, moist dressings are applied under aseptic conditions. If the incisions are adequate, rubber-tissue drains may be omitted in twenty-four to forty-eight hours. Hospitalization until the infection subsides is of paramount importance.

Sulfonamides are administered, sulfadiazine being the drug of choice. Since the advent of sulfonamide treatment in purulent tenosynovitis there has been no great decrease in the incidence of tendon slough. This is apparently due to the time factor. With septic tenosynovitis existing for forty-eight to seventy-two hours, it is obvious that the sulfonamides cannot be a great factor in

correcting physiologic changes that have occurred in blood vessels, pathologic changes in the involved tissues or mechanical changes in the tendon sheaths. Despite the fact that there has been no appreciable change in the incidence of sloughed tendons with sulfonamide therapy, there has been a decided decrease in the incidence of other severe complications in septic tenosynovitis.

DEEP FASCIAL-SPACE ABSCESS

The fascial and aponeurotic strata of the hand, especially in their formation of important surgical spaces, have been inadequately or improperly described in textbooks and the anatomical literature up to the time of Kanavel.

Kanavel,³ after multiple dissections and injections, described the deep fascial spaces—that is the midpalmar and thenar spaces. He stated that these two spaces are separated in the palm by a fascial septum that arises from the undersurface of the flexor tendon of the middle finger and fuses with the fibrous tissue overlying the middle metacarpal bone.

Brickel,²⁰ in 1939, stated that in all his dissections and injections he never found a special palmar septum extending from beneath the flexor tendons to the middle metacarpal bone, dividing the palmar space in halves. Thus, he stated, it is justifiable to discard the concept of a midpalmar space in favor of a broader interpretation of its boundaries, and to discard the term "thenar space" in favor of the term "abductor space, anterior and posterior." I believe that Brickel's observations and conclusions are wrong.

Anson and Ashley,²¹ in 1940, dissected many hands with special consideration of the fascial distribution. Their report, however, was inconclusive so far as the existence of the important surgical fascial spaces in the palm is concerned.

Because of the confusion concerning the existence of important surgical fascial spaces in the hand, I²² dissected 100 hands with special consideration of the fascial distribution. In all the cases there was a definite septum of fascia coming from the undersurface of the flexor tendon of the middle finger, which was attached to the entire length of the middle metacarpal bone. This septum divided the palm into two main fascial spaces, and in no case was it possible to insert a probe beneath the flexor tendons in the proximal half of the palm and move it from side to side without meeting obstruction. Furthermore, in no case was a direct communication between the midpalmar and thenar spaces found.

Anatomical dissection of the fascia of these hands revealed that there are definite midpalmar and thenar spaces. The midpalmar space extends

from the middle metacarpal bone ulnaward to the radial side of the metacarpal bone of the little finger. Anteriorly, this space is bounded by the flexor tendons of the middle, ring and little fingers, the third and fourth lumbrical muscles and the thin fascia that connects these tendons and muscles.

The posterior boundary or floor is formed by the fascia covering the second and third volar interosseous muscles and the third, fourth and fifth metacarpal bones. In the distal third of the floor, small compartments are formed, since septums coming from the undersurface of the palmar aponeurosis are attached to the fascia of the volar interosseous muscles. These small compartments communicate with the midpalmar space. The medial boundary is the fascia on the radial side of the hypothenar muscles. The lateral boundary is the midpalmar septum, which extends from the undersurface of the flexor digitorum profundus tendon of the middle finger to the middle metacarpal bone. Distally, the midpalmar space extends to about 2 cm. proximally to the webs. The distal boundary is composed mainly of fascial septums extending from the palmar aponeurosis to the floor of the space and to some transverse fasciculi. The proximal boundary is a thin fascial septum usually found at about the level of the proximal end of the transverse carpal ligament. Clinically, however, abscesses do not usually enter the carpal tunnel. This fact is probably due to tissue response to infections—that is, serous, cellular and fibrinous reactions.

The thenar space is bounded posteriorly by the adductor pollicis muscle. Medially, the boundary is the midpalmar septum, a thin fascia extending from beneath the flexor digitorum profundus tendon of the middle finger to the third metacarpal bone. Proximally, in all cases, this fascia, which is part of the adductor fascia, forms the boundary. This proximal boundary is found at about the level of the distal end of the transverse carpal ligament. The anterior boundary or roof is the thin layer of fascia formed as the midpalmar septum splits and courses laterally. In its lateral course this roof ensheaths the flexor tendons of the index finger to form part of the anterior boundary. The lateral boundary of the thenar space is formed by the thin fascia as it extends over the lateral edge of the adductor pollicis muscle and is attached to the dorsal aspect of this muscle. This distribution of fascia over the anterior, lateral and dorsal aspects of the adductor pollicis muscle clearly indicates why abscesses of the thenar space may extend to the posterior aspect of the muscle. The fact re-

mains, however, that abscesses of the space tend to remain anterior to the adductor pollicis muscle.

Bunnell²³ stated that the midpalmar septum is so thin it is of questionable surgical value. In all my dissections there was an involvement of midpalmar and thenar spaces in only 2 cases, and this occurred after extensive local necrosis in which even osteomyelitis was found.

The symptomatology and differential signs of deep fascial-space abscesses are well known. In thenar-space abscess, there is tenderness over the palmar aspect of the thenar space. In midpalmar-space abscess, there is tenderness over the palmar aspect of the midpalmar space. Swelling is significant. In midpalmar-space abscess there is obliteration of the concavity of the palm and a slight bulge over it. In thenar-space abscess there is usually a rapid increase in size of the thenar area: the tissues seem to balloon out from the radial longitudinal crease of the palm. In both infections there is usually great swelling over the dorsum of the hand. The position of the fingers is of some diagnostic value. The middle and ring fingers are flexed when the midpalmar space is involved. The index finger is usually flexed when the thenar space is involved. The temperature for each infection ranges from 100 to 104°F. Midpalmar space abscess is relatively rare.

Other attempts at description of the symptomatology of the deep fascial-space infections have been made in the past few years. These descriptions have added nothing but confusion. It should be repeated, however, that a definite diagnosis must be made from history and physical examination before surgery is attempted.

Various incisions have been made in thenar-space abscess. Some earlier surgeons made a through-and-through opening from the palm to the dorsum. This incision is to be deprecated. It is followed by contractures, deformities and deranged function, and often new channels for infection are opened. Incisions over the volar aspect of the thenar eminence may cut across the proximal transverse crease and cause later contractures. Kanavel³ was the first to show that adequate drainage can be obtained with an incision over the dorsum of the thumb-index web, and that a scar on the palm is thus avoided. Brickel²⁰ suggested an incision over the palmar edge of the first dorsal interosseous muscle. However, a large branch of the radial artery may be cut at the proximal end of the wound.

The incision for thenar-space abscess should drain pus, which may be found either volar to the abductor pollicis muscle or on both its volar and dorsal aspects. The incision of choice is made over the dorsum of the thumb-index web,

at the middle of a line drawn between the distal ends of the metacarpal bones of the thumb and index fingers, with the thumb in a position of abduction.

In midpalmar-space abscess various incisions have been used. Through-and-through incisions, employed by some surgeons even fifteen years ago, should be strongly condemned. If one remembers that the cellular tissue on the dorsum of the hand is loose, that edema of the dorsum is constantly found with infections involving the volar surface of the finger or palm, and that the lymphatics take the shortest route to the dorsum of the hand, a through-and-through incision will not be made. Spread of infection and contractures are certain to follow if an incision is made through the volar skin, midpalmar space, volar interosseous fascia, interosseous muscles, dorsal interosseous fascia, dorsal aponeurosis, subcutaneous tissue and dorsal skin.

Volar longitudinal incisions have been made, cutting across the proximal and distal transverse creases of the palm. These incisions are condemned because contractures follow.

Kanavel³ first suggested that a vertical incision be made between the middle and ring fingers or between the ring and little fingers, with the idea that such incisions in addition to giving direct access to the midpalmar space would afford more adequate drainage of an involved lumbrical space and be associated with less risk of injury to the digital nerves and blood vessels.

Bunnell²³ first emphasized the danger of contracture resulting from vertical scars. Such contractures are found when the incisions completely divide the web or when the incision is carried too far proximally in the palm. Various types of transverse incisions have been described.

The incision of choice for midpalmar space abscess is a transverse incision through the distal transverse crease or on a line parallel with the distal transverse crease, or over the center of convexity of the palm. This incision is carried transversely through the skin, superficial fascia,

and palmar aponeurosis. The digital vessels and nerves are identified and retracted with the flexor tendons. Usually a point between the flexor tendons of middle and ring fingers is entered. This latter incision is placed longitudinally through the thin subaponeurotic fascia between the flexor tendons, and enters the midpalmar space.

Sulfonamides, particularly sulfadiazine, are of value in decreasing the incidence and complications of deep fascial-space abscess.

Postoperatively, one must diligently adhere to elevation of the hand, splinting in a position of function, hospitalization with local and systemic rest, warm moist dressings under aseptic conditions, proper diet and adequate intake of fluid

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 29491

PRESENTATION OF CASE

A sixty-eight-year-old housewife entered the hospital because of chills and fever of forty years' duration.

About forty years before entry the patient began to have intermittent bouts of chills and fever. The chills were severe and shaking in character, lasted an hour and a half and were followed by fever and profuse sweating. They occurred two or three times a year and occasioned no alarm. No treatment was deemed necessary. She lived in New England at that time and had not been elsewhere. About eleven months before entry the chills increased in frequency, ranging between two times a week and once in ten days. The chills lasted up to an hour, were followed by fever of 104°F. and profuse sweats. The attacks were followed by prostration lasting for a day or two. During an attack the systolic blood pressure fluctuated between 210 and 110. Seven months before admission the patient went to Florida, where, during the course of one of the attacks, a physician found the blood "teeming with malarial parasites." She was given atabrine, sulfathiazole and barbitol without relief. She returned to New England. The symptoms persisted and seemed to increase in severity. Her family physician was unable to find any parasites in the blood.

Six months before entry the patient was noted to have jaundice. The urine was dark, but the stools were normal in color. It is not stated how long the jaundice lasted or how severe it was, but it gradually cleared up. For the four weeks preceding admission, the chills and fever occurred at weekly intervals. There had been a weight loss of 50 pounds in the past year. Some nausea and vomiting of watery material were present occasionally after chills, as well as a mild pain across the upper abdomen. There was occasional dysuria, and some low back pain. The patient was said to have lived "on an inadequate bland diet because of ulcers diagnosed ten years before

entry," but no additional information was available.

The patient had had a complete hysterectomy at thirty-seven for fibroids and a right radical mastectomy at fifty-four for carcinoma. Her father was said to have had a similar illness with severe shaking chills, aches and fever, which had been contracted in the South during the Civil War and was thought to be malaria. He died, however, from massive gastric hemorrhage.

Physical examination showed a well-developed and well-nourished woman lying quietly in bed. Numerous senile keratoses were seen below the breasts. The scars of the mastectomy and the hysterectomy were well healed. There was no superficial evidence of recurrence of the carcinoma. The pupils were round and equal and reacted to light and accommodation. The sclerae were clear. There were tortuosity and narrowing of the fundal vessels, with arteriovenous nicking. The nasal septum was perforated, the hole being 0.5 cm. in diameter; the location of the perforation was not given. The lungs were clear. The heart was of normal size, the sounds were of good quality and regular. There were no palpable organs, masses or tenderness in the abdomen.

The blood pressure was 170 systolic, 70 diastolic. The temperature was 100.4°F., the pulse 88 and the respirations 20.

Examination of the blood showed a red-cell count of 4,360,000 with 12.8 gm. of hemoglobin. The white-cell count was 12,900 with 86 per cent neutrophils. A blood Hinton test was negative. The icteric index was 5. Repeated blood smears failed to show malarial parasites. The urine was light brown, with a specific gravity of 1.008 and a + test for albumin; the sediment showed occasional red cells, 8 white cells and 10 epithelial cells per high-power field. The culture was negative. The stools were light brown and guaiac negative. A stool culture was overgrown by a proteus bacillus.

X-ray examination of the chest showed the lung fields to be clear except for a small area of calcification in the region of the lower lung field. There was no evidence of metastatic cancer in the bones of the shoulder girdle. The diaphragm was smooth. The heart was not remarkable. An intravenous pyelogram was negative. Two Graham tests failed to show concentration of the dye in the gall bladder.

On the third hospital day an abdominal exploration was performed.

DIFFERENTIAL DIAGNOSIS

DR. CHESTER M. JONES: It has been a long time since I have read a case protocol that presents so

*On leave of absence

many points of uncertainty. I am sure that I cannot make an absolute diagnosis. There are many discordant statements, which make a diagnosis difficult. One is the fact that the patient's physician found her blood "teeming with malarial parasites." This was not substantiated, but the examination was done in the South where such procedures should be adequately carried out. Secondly, the patient had a previous history of cancer of the breast. Thirdly, the nasal septum was perforated. Whether these facts have any bearing on the present situation is a question. I am inclined to think they do not. It is hard to forget all of them, however. The physical examination, except for evidence of arteriosclerosis and a perforated septum, was absolutely negative. Nothing was felt or found on auscultation or inspection that gave a clue concerning the existence of organic disease. The only evidence is the story of chills and fever, plus the fact that on two x-ray examinations the gall bladder failed to fill with dye. It is hard to correlate this paucity of facts with a story of about forty years of chills and fever.

What are the things that could give chills and fever of that duration? Obviously chronic infection has to be considered. One may properly ask the question whether these episodes of chills and fever that had occurred for thirty-nine years were the same things that were occurring during the eleven months before entry. There is no reason for saying that they are not, but that is a long duration of episodes that are preceded by rigor. In 1900, malaria was prevalent in and around Boston. I do not know where this patient lived, but if she lived around the Charles River Basin at that time she could have had it.

DR. BENJAMIN CASTLEMAN: She lived on the North Shore.

DR. JONES: I am not at all sure that there was malaria at that distance from Boston, but the story of malaria for forty years does not ring true. The Florida physician who found the parasites was not able to control the chills and fever with atabrine, a drug that should have a definite action on the parasites. There is every indication that adequate doses of atabrine should control the chills and fever of malaria. Whether or not sulfadiazine would have been effective is a question. She had chills and fever here, and malarial parasites were looked for, both in the hospital and outside, but none were found. It seems to me that even if she had had malaria in the past, this disease was not the condition that was productive of the recurrent chills and fever that brought this woman eventually into the hospital. I am not

aware of any other parasitic manifestation that will cause recurrent chills and fever of this sort except amebiasis. It is conceivable that she might have had an amebic infestation followed by intrahepatic disease with abscess formation, which could have caused chills and fever for a long period of time. I do not know how far back a story of recurrent chills and fever on the basis of amebic abscess can go, but I know of one patient with an amebic abscess that caused symptoms twenty years after the original infestation. Here we have a story of chills and fever that began forty years ago and constantly recurred. It seems inconceivable to me that amebic abscess of the liver was the basis of the patient's difficulty. One fact that conceivably may help us here is that her father was in the Civil War and had something that caused diarrhea and chills, which also was thought to be malaria. Of course there was plenty of dysentery of the bacillary and amebic types in the Civil War. He might have been a carrier and contributed the source of the amebic infestation. I have no enthusiasm for that as a diagnosis in this case. The duration was too long, and after such a period it is surprising that there were no physical signs of liver involvement other than the fact that she was jaundiced on one occasion some months before she came into the hospital.

If it was not a parasitic infestation, was it a bacterial infection? What are the infections that persist for forty years and cause chills and fever? Osteomyelitis, undulant fever, tuberculosis and possibly endocarditis might cause chills and fever for a year prior to admission or perhaps a little longer, but hardly for forty years. We have no evidence clinically of tuberculosis, undulant fever or endocarditis. Chills and fever are sometimes due to an intermittent blockage of the ball-valve type of the ureter or renal pelvis causing hydro-nephrosis, or of the cystic or common duct. That does happen with ureteral stones, with a stone in the pelvis of the kidney and with gallstones either in the cystic duct near the ampulla of the gall bladder or in the common duct. Of course as a rule these are associated with attacks of pain, but I can recall certain patients with chronic cholecystitis and stones who, from time to time, had recurrent episodes of chills and fever without any pain whatever. We know that this patient had these symptoms for a long time. We also know that her father, with whom she presumably lived, was very sick with chills and fever and diarrhea during the Civil War. I do not want to draw too much on that lead. On the other hand, typhoid fever was frequent; he might have been a typhoid carrier, and she might have had

a mild attack of typhoid fever, with residual infection in the gall bladder. These are conceivable probabilities but not at all clear, and certainly I have a great deal of difficulty in accepting any as a logical explanation of what brought this patient to the hospital.

In trying to reconstruct this case it seems to me that of the possibilities I have mentioned, a stone in the gall bladder that occasionally went down into the cystic duct and caused obstruction to the flow of bile from the gall bladder and infection, possibly with cholangitis, might answer the requirements for a diagnosis going back forty years. It is entirely possible that she could have had a real cholecystitis at twenty-eight years of age. I am inclined to suggest that as the only reasonable explanation of this history. It is backed up by the two x-ray films in which the gall bladder failed to fill. If the test was done properly, and no evidence of duodenal ulcer, intrahepatic disease or diarrhea was present, then such findings mean a nonfunctioning gall bladder.

As a remote cause of recurrent chills and fever, one might mention recurrent thrombophlebitis. I do not believe that the patient had it. Similarly, I do not believe that the patient had liver abscess. The perforation of the nasal septum could have been due to syphilis; but the evidence is against it. It may have followed a submucous resection, which was a frequent occurrence some years ago. I do not believe this patient had metastatic cancer. It could not explain forty years of chills and fever, nor could it explain eleven months of chills and fever in the absence of physical signs anywhere. Therefore I shall abide by a diagnosis of cholecystitis with stones in the common duct.

CLINICAL DIAGNOSES

Charcot's intermittent hepatic fever.
Cholecystitis.

DR. JONES'S DIAGNOSES

Chronic cholecystitis.
Cholelithiasis.

ANATOMICAL DIAGNOSES

Chronic cholecystitis.
Cholelithiasis.
Choledocholithiasis.
Cholecyst-duodenal fistula.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Dr. Roger I. Lee saw this patient before operation and his note reads, "History and findings strongly suggest Charcot's intermittent hepatic fever." Dr. Arthur W. Allen operated on this patient and I shall read part of his operative note.

The liver was slightly darker than normal. The omentum was adherent to the under surface of the liver. It was freed with some difficulty by sharp dissection. As the operative site was further developed it became apparent that there was a cholecyst-duodenal fistula. The gall bladder itself was of normal size but its wall was markedly thickened. The fistula measured approximately 2 cm. across. Before division of the wall of the fistula it was thought wise to expose and explore the common duct. The ampulla and cystic ducts were developed, and finally the common duct was exposed. The latter measured 2.5 to 3 cm. across, and its wall was 2 mm. thick. The duct was opened, and there was an immediate gush of thick bile and numerous, black, friable, mushy stones. The distal centimeter of duct was packed with this sediment. A generous opening was made in the duct, and the sediment was removed with a scoop. The duct was finally irrigated with saline through a catheter.

After it had been ascertained that the obstruction was of a benign nature, the cholecyst-duodenal fistula was dissected. A finger could then be inserted into the duodenum, and the ampulla was accurately identified. The common duct was probed with this exposure, and the ampulla admitted a 3-mm. dilator snugly. Dilation was carried out through the 9-mm. dilator. The left and right hepatic ducts were calibrated, the right duct admitting a 7-mm. dilator.

The gall bladder was next removed from above down. The cystic duct was only slightly dilated. A No. 16 T tube was then sutured into the common duct, and a watertight closure was accomplished. Finally the duodenal defect was closed transversely, using two rows of catgut, reinforced with a third row of interrupted cotton.

This patient, therefore, had chronic gall-bladder disease for forty years, and each time one or more stones entered the fistula a block occurred that caused chills and fever; when the stones went through into the duodenum, she was relieved.

DR. JONES: At one time there must have been a stone impacted in the cystic duct with empyema of the gall bladder, because the perforation into the duodenum must have occurred while the cystic duct was blocked.

DR. CASTLEMAN: She remained in the hospital three weeks following the operation, free from fever and chills, and then went home.

DR. JONES: Were the stones cultured?

DR. CASTLEMAN: Yes, and the cultures showed only colon bacilli.

CASE 29492

PRESENTATION OF CASE

First admission. A thirty-six-year-old American laborer was admitted complaining of pain in the chest.

About two years before entry, while lying in bed, the patient was suddenly seized with a severe pain in the left chest that radiated down the left

arm. The pain lasted about four hours and was very severe. At intervals thereafter he noted a vague sensation of pressure in the chest and moderate dyspnea on exertion. About two weeks before entry he had a severe attack of pain in the chest and left arm, which occurred during the night and lasted about an hour. The pain was less severe when he sat up, and was associated with a moderate amount of gaseous eructation. A sedative afforded relief and he was able to fall asleep. Shortly afterward he again awoke and voided a large amount of urine. On the following day he visited the Out Patient Department, where a general physical examination was said to be negative; the blood pressure was 135 systolic, 80 diastolic. A blood Hinton test was negative, and an x-ray film of the chest showed the lung fields to be clear. The heart was at the upper limit of normal in its transverse diameter and showed slight relative increase in the size of the left ventricle. The supracardiac shadow was normal, and the trachea was not displaced. An electrocardiogram was entirely negative. About a week before entry, in the afternoon while sitting at his work, the patient had another attack. This began as a sudden sensation of soreness in the left chest but was not severe enough to cause him to stop work. On his way home, however, he had a severe attack, during which he could do nothing but stand still for a minute or two. The pain at that time radiated down the left arm. He was compelled to take a taxi and on arriving home attempted to climb four flights of stairs, but was unable to do so. A physician administered some tablets that produced relief. The patient then tried to continue up the stairs but was compelled to stop frequently and finally succeeded in reaching his apartment after thirty-five minutes. He then lay down and went to sleep. The following morning he felt weak but was able to get up and go to work. During the succeeding week he had three minor attacks of chest pain and another very severe one, during which he entered the Emergency Ward. The last attack followed notification that his salary would be cut.

Examination showed a well-developed and well-nourished man lying flat in bed in no evident discomfort. There were no abnormal physical signs. The lungs were clear. The apex impulse of the heart was seen and felt in the fifth interspace in the midclavicular line. There were no murmurs.

The blood pressure was 120 systolic, 70 diastolic. The temperature, pulse and respirations were normal.

Examination of the urine was negative. The blood showed a red-cell count of 4,500,000, with a hemoglobin of 75 per cent. The white-cell count

was 8800, with 71 per cent neutrophils. The stools were essentially negative. An electrocardiogram showed a PR interval of 0.16 second with normal rhythm; T_1 was low and slightly inverted, T_2 , T_3 and T_4 were upright, and Q_1 was present. A Graham test and a gastrointestinal series were negative.

Six days later another electrocardiogram showed a late inversion of T_1 ; T_2 and T_3 were upright, with a slightly high origin. The patient's condition remained good through his hospital stay, and on bed rest he exhibited no discomfort. On the twentieth hospital day another electrocardiogram showed a slightly low T_1 , which, however, was practically within normal limits; T_2 , T_3 and T_4 were upright, T_1 was diphasic, and Q_1 was markedly shortened. He was discharged on the twenty-fourth hospital day.

Second admission (one and a half months later). The patient was followed in the Out Patient Department, where he complained of recurrent attacks of vague pain, always following mild exertion. The pain occurred in the left chest and frequently radiated down the left arm. An electrocardiogram taken two weeks after discharge showed a low T_1 , an upright T_4 and an M-shaped QRS. One and a half months after discharge he was seized with substernal pain that was much severer than usual. It lasted for about an hour and was replaced by a dull constant ache in the chest and left arm. He went to sleep afterward and was suddenly awakened by a severe upper retrosternal squeezing pain even severer than the previous pain. There was an aching sensation in the left arm and jaw, and a splitting headache, and the patient was unable to lie back without aggravating the pain in his chest. He was placed in a taxi and immediately brought to the Emergency Ward.

Physical examination was again essentially negative. The heart was not enlarged but the sounds were distant in character.

The blood pressure was 110 systolic, 90 diastolic. The temperature was normal. The pulse and respirations were not recorded.

The blood showed a white-cell count of 10,000. He continued to have substernal pain and vomited once after entry. Four hours later a few in constant rales were heard at the bases of the lungs, but there was no change in his condition. The temperature remained normal. Although no significant change had been noted in his general condition, the patient suddenly died eight hours after entry.

DIFFERENTIAL DIAGNOSIS

DR. CONGER WILLIAMS: This case concerns a man of thirty-six with a history of recurrent at-

racks of severe pain in the chest radiating down the left arm. He ultimately died, following one of the attacks two years after the onset of symptoms. In spite of the age of the patient the diagnosis of coronary heart disease with angina pectoris and myocardial infarction seems the best possibility. The pain was located in the left chest during the first few episodes but was later described as recurring in the substernal region. The pain of coronary insufficiency or myocardial infarction is usually located in the sternal region but may occur to the right or the left of it.

The negative findings on physical examination and electrocardiogram the day following the first attack do not exclude either myocardial infarction or coronary insufficiency. On admission to the hospital two weeks later, after recurrent episodes of pain in the chest and arm, the electrocardiogram was definitely abnormal, with an inverted T wave in Lead 1 and a Q wave in Lead 4. Six days later the T wave in Lead 1 was more deeply inverted. These electrocardiographic changes, especially the presence of a Q wave in Lead 4, are practically diagnostic of myocardial infarction, provided that the Q wave was of significant size. It would be helpful to see the electrocardiograms in this case, but they are not available. Apparent changes in the QRS complexes toward a more normal pattern during the first admission do not necessarily point against the diagnosis, since such changes may occur with minor differences in placing of the chest electrode at the apex. Furthermore, the T wave in the apical lead may be upright in an anterior infarction, with significant changes occurring either to the right or to the left of the apex.

I believe that at the time of the first hospital admission the patient had had several episodes of coronary insufficiency and probably at least one myocardial infarction. In the interval between admissions pain was present only on effort, further evidence in support of a diagnosis of coronary heart disease. The patient died eight hours after the onset of the final episode with symptoms suggesting myocardial infarction. His sudden death can therefore be explained by the onset of ventricular fibrillation.

Another possibility that must be considered is rupture of one of the coronary arteries, with death resulting from acute pericardial tamponade. Death does not necessarily occur immediately, but may follow in several hours, depending on the size of the break. The blood-pressure change, with the low systolic pressure and a narrow pulse pressure, is consistent with such a diagnosis, but no mention was made of dyspnea or distended neck veins, although the latter finding might have been missed after admission. Myocardial rupture must

also be considered, but is most unusual only eight hours after the onset of an infarction.

There are several other possibilities, but I believe that coronary heart disease with recurrent myocardial infarction and angina pectoris is the only diagnosis that fits all the findings. Dissecting aneurysm of the aorta can produce pain of this type, but repeated episodes over a period of two years are hardly in keeping with the nature of the lesion, and the absence of hypertension is against it. Syphilitic aortitis with narrowing of the mouths of the coronary arteries may produce coronary insufficiency at an early age, but it is hardly in keeping with a history of prolonged episodes of pain suggesting infarction. Furthermore, the blood Hinton test was negative. The nature of the pain does not suggest saccular aneurysm of the aorta, and negative x-ray films dispose of this suggestion.

Other possibilities that might be considered briefly are mediastinal emphysema, pneumothorax and pulmonary embolism, but there is no evidence to support any of these diagnoses. Thus, I am left with only the diagnosis of coronary heart disease. Because of the patient's age one should raise the question of a systemic disease that produced involvement of the coronary arteries as one of its manifestations. Occasionally such a condition accounts for involvement of the coronary arteries in young people. Syphilis has already been considered and rejected. Xanthomatosis is a possibility, but no mention was made of splenic or hepatic enlargement, the blood cholesterol level was not studied, and no skin nodules were reported. Periarteritis nodosa and Buerger's disease are other conditions to be considered, but again there is no supporting evidence.

CLINICAL DIAGNOSES

- Coronary thrombosis.
- Coronary heart disease.

DR. WILLIAMS'S DIAGNOSES

- Coronary heart disease with myocardial infarction (? anterior).
- Ruptured coronary artery with pericardial tamponade?
- Angina pectoris.

ANATOMICAL DIAGNOSES

- Coronary thrombosis, recent, right.
- Coronary thrombosis, old, left descending and circumflex branches.
- Myocardial infarction, old.
- Myocardial fibrosis.
- Arteriosclerosis, marked, coronary and aortic.
- Hydrothorax, slight, bilateral.
- Pulmonary edema.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: This patient did have severe coronary heart disease. Both main vessels were markedly atherosclerotic and calcified. There was an old thrombotic occlusion 3 cm. in length beginning a few millimeters beyond the origin of the left main coronary artery and another similar occlusion of the left circumflex branch near its origin. Most of the blood supplying the heart, therefore, must have been coming via the right coronary artery. This vessel was markedly narrowed in a few places but still patent except for one point about 4 cm. from its origin

where there was a recent thrombus completely occluding the lumen. This was undoubtedly the cause of the last substernal attack that led to death. There was an old myocardial infarct involving the septum and anterior wall of the left ventricle, and scattered small foci of fibrosis in the rest of the heart, but no definite evidence of acute infarction. Eight hours is too short a period for one to be absolutely sure of changes in the myocardial fibers, and unless numerous sections were taken from various parts of the heart, a small area of acute infarction might be missed. The heart weighed only 325 gm. and was not hypertrophied. There was no hemopericardium

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EPIDEMIC INFLUENZA

EACH fall and winter following mobilization for this war there has been an increasing expectancy and uneasiness concerning the possibility of a recurrence of a pandemic of influenza similar to what occurred in 1918. This anxiety stems from the natural fear that such a pandemic might again take a tremendous toll of human life both in and out of the armed forces and that, in addition, it might so cripple temporarily both the battle and production fronts that it would necessitate alterations in the present schedules aimed at the successful termination of the war at the earliest possible date. Furthermore, all those concerned

are only too well aware of the unhappy fact that although much has been learned about the etiology of influenza since 1918, little specific information has been acquired that offers hope of altering in any way the course of such an outbreak or even much hope of altering the outcome in individual cases.

During the past decade viruses have been recovered from circumscribed epidemics of influenza. The commonest of these is designated as influenza A, and another is called influenza B. A third and related virus has been isolated from swine during an epizootic of influenza in this species. The characteristics of these viruses are now fairly well known. It is not known, however, whether these viruses are in any way related to the causative agent of the pandemic of influenza of 1918.

The last epidemic of influenza of any significant proportions occurred during the fall and winter of 1940-1941. At that time, influenza A was found to be the infecting virus in many parts of the United States, as well as in other countries.^{1,2} Similar outbreaks occurring in various parts of Canada have been studied since that time. Two of the latter have been identified as due to influenza A and one as probably due to influenza B.^{3,4} In one of the recent outbreaks of influenza A infection, vaccination with this virus was found to be totally ineffective as a prophylactic measure. All the outbreaks that have been studied since the new viruses were discovered have been relatively mild and have been associated with an extremely low mortality. In view of the fact that epidemics of influenza are prone to recur at two-year to three-year intervals, it is not unreasonable to expect an outbreak in this country during the present season.

A number of considerations lead one to believe that any epidemic in the near future is likely to be much less severe than was the pandemic of 1918. This, of course, is only speculation but is based on significant observations. In the first place, the influenza of the last war, at least in the Army camps from which complete reports are

available, was associated with a high mortality, but the deaths were accounted for chiefly by complicating pneumonias, in which the hemolytic streptococcus was the organism most frequently encountered. Other organisms, including the Pfeiffer bacillus and *Staphylococcus aureus*, were also involved. A similar high mortality accompanied the epidemics of measles that occurred in the same Army camps, and the mortality from this disease was also attributable chiefly, if not entirely, to the complicating hemolytic-streptococcus pneumonias.

During the 1940-1941 influenza outbreak, the staphylococcus played an important role in the complicating pneumonias, both in Boston and elsewhere.^{1,2} The results of intensive treatment of the complicating pneumonias with sulfadiazine and sulfathiazole were quite encouraging, and it was suggested that, should another outbreak of influenza occur, it might well prove useful to employ these sulfonamides in severe cases. This was particularly advocated in patients with severe prostration who had the signs or symptoms of tracheo-bronchial and pulmonary involvement, especially those in whom bacteriologic examination of the sputum had revealed the presence of hemolytic streptococci and staphylococci in appreciable numbers. In such cases, intensive treatment begun early and continued from three to five days might be expected to prevent an appreciable number of the fatal pulmonary complications. More prolonged therapy would be necessary, however, if the bacterial infection had already become established.

Another encouraging omen, which possibly has a more direct bearing, comes from the recent reports concerning measles. During the past year, outbreaks of this disease have occurred in the Army, but deaths from this cause have been rare.³ The low mortality may be directly attributable to the widespread use of sulfonamide drugs in all cases having pulmonary complications, and it is not unreasonable to expect a similarly low fatality

rate from influenza occurring under like circumstances.

From recent observations, particularly those made in the 1940-1941 epidemic, one may also expect that the staphylococcus will play a considerably greater role than in any of the previous epidemics. The increased frequency with which this organism is being encountered in complications of other respiratory diseases, as well as in surgical conditions, strengthens this possibility. The use of penicillin in staphylococcal pneumonias that occur as a complication of influenza would, of course, be most desirable; but the limited supply of this agent will probably preclude its employment on a large scale, at least during the coming season.

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BOOK REVIEWS

THE question whether book reviews should be signed or initialed or should remain anonymous has been discussed many times at meetings of the editorial board of the *Journal* during the past several years. Owing to a letter published in the November 4 issue of the *Journal*, the matter has again been considered by the board, as well as by the Committee on Publications of the Massachusetts Medical Society.

It is obvious that a book review, to fulfill its function, must present to the reader the true opinion of the reviewer concerning the value of the book. If the latter is required to append his name or initials, he is likely to be less frank in his criticism of a book whose merit he questions, particularly if the author happens to be well known. On the other hand, anonymity permits unjust, possibly prejudiced, criticism, whereas the signed name

or initials often enable the reader to judge whether the reviewer is qualified to pass judgment on the book in question. That both sides of the question have supporters is evidenced by the fact that some medical periodicals have adopted one policy, whereas the remainder have selected the other.

During the many years that the *Journal* has been the official organ of the Massachusetts Medical Society the members of the editorial board have always been of the opinion that an anonymous review is likely to be more truly informative and useful than one that is signed or initialed. Furthermore, at recent meetings of the board and of the Committee on Publications, both bodies voted unanimously to continue this policy, with the added provision that the anonymity shall be absolute—in other words, that the name of the reviewer shall not be revealed on inquiry. This, of course, places considerable responsibility on the editorial staff, inasmuch as properly qualified reviewers must be selected and unjust criticism must be deleted. Such accountability, however, is nothing new and will continue to be accepted by the staff, with the earnest hope that it can be properly met.

MEDICAL EPONYM

MENDELIAN LAW

The law that the type of one or other parent is predominant in hybrid progeny is one of the implications arising from the extensive experiments of the Austrian monk, Gregor Johann Mendel (1822-1884). A summary of Mendel's experiments was printed in the *Verhandlungen des Naturforschenden Vereines in Brünn* (4: 1865, 1866), under the title "Versuche über Pflanzen-Hybriden [Experiments in Plant Hybridization]." The extract translated below was taken from a reprint of the original article and appears in *Verhandlungen des Naturforschenden Vereines in Brünn* (49: 3-47, 1911); the following is found on page 24:

An important clue is offered by the fact that in *Pisum* [the pea] constant forms appear among the progeny of hybrids in every combination of associated characters. So far as our experience goes, we find it universally true that constant progeny can be formed only if both

the germ cells and the fertilized pollen are endowed with the capacity to produce identically similar individuals, as occurs in the normal fertilization of pure varieties. Therefore, we must also regard it as necessary that, in the production of constant forms by hybrid plants, completely similar factors must be working together. Inasmuch as the various constant forms are produced by *one* plant or even by *one* of its blossoms, the conclusion seems logical that there are formed in the ovaries of hybrids as many kinds of germ cells [germinal vesicles], and in their anthers as many kinds of pollen cells, as there are possible constant combination forms, and that these germ and pollen cells in accordance with their essential nature, correspond to individual forms.

In fact it can be shown theoretically that if we assume that the different kinds of germ and pollen cells are formed in the hybrids on the average in equal numbers, this hypothesis would be entirely adequate to explain the development of hybrids in single generations.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

GAGE—JAMES A. GAGE, M.D., of Lowell, died November 29. He was in his eighty-sixth year.

Dr. Gage received his degree from Harvard Medical School in 1885. For many years, he was staff surgeon at the Lowell General Hospital until he retired from active practice in 1930. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives.

GIVAN—LIEUTENANT COMMANDER JAMES A. GIVAN (MC), U.S.N.R., formerly of Worcester, died November 14 at the United States Naval Hospital, Norfolk, Virginia. He was in his forty-fourth year.

Dr. Givan received his degree from Tufts College Medical School in 1922. He was appointed to the staff of the Worcester City Hospital in September, 1925, and rose to the post of assistant orthopedic surgeon. He had practiced orthopedic surgery in Worcester for over fifteen years when he entered the Navy in August, 1942. At the time of his death he was chief of the orthopedic staff at the hospital of the Naval Operations Base at Norfolk. He was a councilor of Tufts Medical Alumni Association and a past president of the Tufts Alumni of Worcester County. He was a member of the Massachusetts Medical Society, American Medical Association, Worcester District Medical Society and Boston Orthopedic Club and a fellow of the American College of Surgeons and American Academy of Orthopedic Surgeons.

His widow, his mother and four children survive.

POTHIER—JOSEPH C. POTHIER, M.D., of New Bedford, died December 1. He was in his seventy-ninth year.

Dr. Pothier received his degree from McGill University faculty of Medicine, Montreal, in 1887. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son, a brother and a sister survive.

SILBERG—MORRIS A. SILBERG, M.D., of Roxbury, died November 20. He was in his fiftieth year.

Dr Silber received his degree from Tufts College Medical School in 1920. He was a member of the Massachusetts Medical Society and the American Medical Association.

A daughter and a son survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

STATIONS FOR DISTRIBUTION OF ANTIPNEUMOCOCCUS SERUM

For the past twelve years, the Department of Public Health has maintained a statewide service for the provision of antiserums for pneumococcal infections. At the height of the demand for serum, in 1939, over nine hundred requests for serum were received. In the last few years the introduction of sulfonamide therapy for pneumonia has changed the situation so that the number of calls for serum has decreased over 90 per cent. Furthermore, the need for serum, when indicated, is no longer as urgent as it formerly was.

In the interests of efficiency and economy, therefore, the department has revised its schedule of depots for serum distribution, of which there were eighty-two at one time. Hereafter, serum furnished by the department will be available only at the following stations:

Types 1-33 inclusive

Boston Bacteriological Laboratory, State House

Types 1, 2, 4, 5, 7, 8, 9, 14 and 18

Holyoke Providence Hospital

Worcester Worcester City Hospital

Types 1, 2, 5, 7 and 8

Haverhill Hale Hospital

New Bedford St. Luke's Hospital

Pittsfield House of Mercy Hospital

Type 1 only

Ayer Ayer Community Memorial Hospital

Beverly Beverly Hospital

Boston Antitoxin and Vaccine Laboratory

Brockton Brockton Hospital

Framingham Framingham-Union Hospital

Gardner Henry Heywood Memorial Hospital

Greenfield Franklin County Hospital

Great Barrington Fairview Hospital

Hyannis Cape Cod Hospital

Lowell St. Joseph's Hospital

Malden Malden Hospital

Nantucket Nantucket Cottage Hospital

Newton Newton Hospital

North Adams North Adams Hospital

Plymouth Jordan Hospital

Quincy Quincy City Hospital

Walpole Pondville State Hospital

Ware Mary Lane Hospital

No changes are being made at this time in the facilities for pneumococcus typing or in the procedure for issuing serum. This procedure may be summed up as follows:

1. The pneumococcus must be typed in a laboratory approved for this diagnostic procedure by the Department of Public Health or in a federal laboratory.

2. The patient must be suffering from clinically diagnosed pneumococcal pneumonia, septicemia, endocarditis, meningitis or peritonitis.

3. In pneumonia, antiserums for Types 1, 2, 4, 5, 7, 8, 9, 14 and 18 are furnished for treatment on identification of the pneumococcus isolated from the sputum. Antiserums for the other types are supplied only when the blood culture is positive. (It is regretted that limited funds necessitate the continued application of the restrictive provision.)

4. In the other infections previously mentioned, antiserums for all types are furnished when pneumococcus is found in the blood, cerebrospinal fluid or peritoneal fluid.

5. In all circumstances antiserum is furnished only with the understanding that any unused serum will be properly refrigerated until the patient is discharged and then will be returned promptly to the Antitoxin and Vaccine Laboratory, 375 South Street, Jamaica Plain, Massachusetts, and that when the patient is discharged, a case history on the form provided will be filled out and sent to the Antitoxin and Vaccine Laboratory.

MISCELLANY

DANGER FROM FLUOROSCOPY

Much used by both internist and surgeon in other fields of medicine, the fluoroscope has proved a valuable aid in the diagnosis of pulmonary lesions and in the periodic check of their progress. A competent examiner using good equipment is often able to secure information that may not be ascertainable by means of conventional films such as the movements of the diaphragm, the contrasting appearance of the expanded or contracted lung, and the effect of moving the thorax into different positions before the screen. Warnings that this method should supplement not replace, good roentgenograms have been frequent. A recent editorial (Stenstrom, K. W. *Danger from Fluorocopy*, *Minnesota Med.* 26:558, 1943) contains a timely warning of another danger—one inherent in the physical properties of the electric current and of the roentgen ray. This safety first appeal merits serious thought.

A number of articles have been published concerning the dangers connected with fluoroscopy. Recent measurements have shown that these warnings must be taken seriously and that they concern the whole medical profession. The problem is more acute now when the serious film shortage may call for more extensive use of the fluoroscopic method and it seems advisable to call attention to a few pertinent facts.

No fluoroscopic unit should be used unless the doctor in charge has convinced himself that the conditions under which it is operated are reasonably safe. A continuous vigilance is necessary, and it is not enough to know that the conditions were satisfactory at one time in the past.

A shock-proofed arrangement should remove electrical dangers but a broken cable or a casual repair may

lead to electrical hazards, and many of the old machines have exposed high-voltage leads. Grounding a part of the apparatus may not always serve as protection, and if the ground is applied at the wrong place the danger may be increased. A careful expert inspection is needed and there can be no valid excuse for an accidental electrocution. Such accidents have occurred a number of times.

Roentgen rays from fluoroscopic units have caused innumerable sequelae to both patients and physicians, and serious damages often still result in spite of the knowledge that now is available.

In order to obtain adequate protection, it is first required that the tube be shielded so that no radiation of any consequence escapes in any direction except in the useful beam. This may be checked roughly with a hand fluoroscope or more accurately with a roentgen meter with a sensitivity of 0.01 r or a Geiger-Muller counter. After this first requirement has been fulfilled several other precautions must be taken.

For any intelligent use of fluoroscopy, it is important to know the amount of roentgen rays reaching the skin of the patient and of the examiner, and that has to be determined by means of measurements. The total dose received depends on the intensity and the time of exposure. The intensity depends on a number of factors and varies widely in practice. A reasonable intensity at the skin of the patient nearest to the tube amounts to about 20 r per minute.

A representative of the Division of Biophysics, University Hospitals, has recently checked some machines in Minnesota, and has found intensities during routine practice up to 114 r per minute. It is evident that such an intensity is dangerous and must be reduced by proper adjustments. The question is how many of the machines which have never been calibrated are used under similar conditions with an unnecessarily high intensity.

The intensity may be reduced by increasing the distance from the target to the patient. This distance should be at least 28 to 30 cm. It can also be reduced by lowering the current, which should not exceed 4 to 5 ma. If the fluorescence is not bright enough the voltage may be raised and it is advisable to use rather high voltage, preferably 80 kv. or 100 kv. if possible with the equipment. With a high voltage a filter helps to lower the intensity considerably and a 1-mm. aluminum filter should be permanently attached.

With the use of a target skin distance of 28 cm., 90 kv., 4 ma., and a 1-mm. aluminum filter, the intensity can undoubtedly be kept within the safe range, but it is still advisable to have it measured so that the number of roentgens applied per minute will be known.

The time used for an examination should be kept at a minimum. It should be measured and recorded. A foot switch should be used so that the current applied to the tube may be limited to the time of inspection. The use of a timer, which sums up the exposure and shuts off the machine when the dose decided on has been given, is advisable.

Some fluoroscopic examinations require an exposure of 5 minutes. With an intensity of 20 r at the patient's skin, this means a dose of 100 r. A dose of 75 r is often used for the treatment of skin diseases, and the title of an article in the *Journal of Radiology*, "Roentgen Therapy in Fluoroscopy," is therefore no exaggeration.

The rules laid down here for the safety of the patient may seem drastic. They are, however, not difficult to follow after they once have been accepted, and certain

ly patients have the right to expect the physician to take the necessary precautions in order to avoid serious injury from a simple examination. These rules also help to protect the examiner, though any injury to him is due to accumulation of exposure over a long time rather than to a single dose. He must be particularly careful to protect the hands, which are inevitably exposed at palpation during the fluoroscopic examination. The use of lead-rubber gloves may help, but not unless the gloves are heavy and designed to shield the whole hand can they be relied on to give complete protection. Light gloves may give a false sense of security. The examiner must in any case be aware of the danger and take all possible precautions.

The most dangerous procedure, and the one that has caused most of the injuries, is the setting of fractures under fluoroscopic visualization. This practice must be condemned and the radiologist in charge should enforce the rule that nobody on the staff be permitted to use the apparatus in this manner. The doctor may receive enough exposure from the setting of a single fracture to produce a severe skin reaction. It is, of course, good practice to inspect the position fluoroscopically and that can be done several times without exceeding the permissible total dose.

A number of physicians already have suffered the consequences of too much exposure during fluoroscopy. They have been severely handicapped, and some have paid with their lives. The tragedy has been extremely impressive, and it is hoped that others will heed the warnings before it is too late.—Reprinted from *Tuberculosis Abstracts* (November, 1943).

REPORT OF MEETING

TRI-DISTRICT MEETING

A joint meeting of the Middlesex East, North and South district medical societies was held on November 10, 1943, at the Boston Medical Library. The presiding officers were the presidents of the district societies,—Dr. Roger M. Burgoyne, Dr. Herbert M. Larrabee, and Dr. Harold G. Giddings,—and the last acted as chairman.

The meeting was called to order at 8:15 p.m. The chairman stated that on the receipt of a telegram from Washington less than a week before, arrangements were promptly made in order to extend the utmost co-operation to the Procurement and Assignment Service, to the medical departments of the Army, Navy and Public Health Service and to Selective Service, which groups had asked that such a meeting be called in the shortest possible time. Dr. Giddings thought that few district medical society meetings had been arranged so quickly, which indicated the willingness of the profession to assist in solving the medical problems of the armed forces. The assembly was then addressed by various persons representing the State and the Government.

Dr. Reginald Fitz, chairman of the Massachusetts Committee of Procurement and Assignment, stated that in 1942 there were approximately 8000 physicians of all ages, including interns and residents, who were practicing in this state and that of this number about 2000 are now in the service.

Dr. Frank Lahey, chairman of the Directing Board of the Procurement and Assignment Service, spoke about the recruitment program. He stated that every man marked "available" is now needed by the military forces

He thought that any physician was privileged to question any other physician concerning how he had been rated. He stated: If a man has been marked essential he can be conscience clear since he has had nothing to do with such a rating. If one so marked wishes to join the service, he must find a substitute, and he may request the Procurement and Assignment Committees to assist him. Dr. Lahey then spoke about the men who had been marked available. He said: If such a person does not agree with his rating he should appeal his classification to the state chairman. He emphasized the fact that a physician who has been marked available and has not sought an appeal indicates by his action that he is disinterested and therefore is truly available for military service. Dr. Lahey then read a copy of a personal letter that he had sent to physicians informing them of the great need and asking them to file their papers for a commission. He further stated that there were about 10,000 physicians in the Navy and about 40,000 in the Army but that the armed forces still needed every available physician who could pass his physical examination.

Lieutenant Colonel Durward Hill, representing the Office of the Surgeon General, spoke about the Army needs. He, like the officers who followed him, brought greetings from the various offices of the Surgeon General. He stated that the Army needed 48,000 medical officers by the end of 1943 and that during 1943 about 1,000 physicians had been released from the service. He spoke forcibly of this need and urged that all available physicians come before the currently organized committee of which he was a member, and present their problems so that appropriate advice could be given.

Commander Francis J. Bracefield from the Bureau of Medicine and Surgery then spoke about and stressed the Navy needs. He said that the Navy was short about 6,000 medical officers, that it would welcome specialists and that physicians even above the draft age would be accepted.

The needs of the United States Public Health Service were then discussed by Dr. John Trautman. A history of the Public Health Service was presented as well as facts pertaining to the increased war services of this branch.

A question period was then conducted by Dr. Paul Barton, assistant executive officer of the Washington Office of the Procurement and Assignment Service. Some of the questions and answers are as follows:

Q What are the present age limits for service in the medical corps of the armed forces?

A The upper limit in the Army is, in general, the forty-fifth birthday, but for specific position vacancies men up to sixty are eligible. The limit in the Navy is, in general, the fiftieth birthday.

Q What is the present status of physical requirements?

A The Navy at the present time still has the highest standards although they are lower than they were. The Army is next and those who are physically disqualified for Army service may be eligible for commission in the United States Public Health Service.

Q What ranks are being offered by the services at the present time?

A The Army is limiting those under thirty-eight to first lieutenancies and those about thirty-eight to captaincies and above if they meet the special requirements of the Surgeon General.

rankings depend on special qualifications. The Navy is limiting those thirty-four and under to lieutenancies, junior grade those from thirty-four to thirty-eight to lieutenancies, and those from thirty-eight to forty-four to lieutenant commanderships. For specific position vacancies requiring special qualifications higher commissions may be offered. The Public Health Service has commissioned ranks similar to those in the Army.

Q What are the present needs of the services?

A All three branches of the armed forces are in immediate dire need of several thousand additional medical officers. This immediate period of need is between now and January 1.

Q What is the Public Health Service classed as one of the branches of the armed forces so far as medical officers are concerned?

A For many reasons among them the fact that they supply the medical personnel for the United States Coast Guard. Physically qualified eligible officers are assigned by the Public Health Service to active duty with the Coast Guard and may be assigned anywhere the American flag flies.

Q Why have so many practitioners who are capable of serving long hours in civilian practice been disqualified for military service?

A The exigencies of service in combat areas are such that civilian practice is no criterion of physical qualification. The services at the present time have a full quota of those whom they can accept for limited duty. They are being forced to discharge some at present. Certain individual physicians who still will be able to undertake heavy civilian duties are no longer able to cope with the needs of combat troops.

Q Why is it necessary for a physician to take an indoctrination course after becoming a medical officer?

A The reason for this is that a physician becomes a medical officer, which means that he is at all times an officer subject to the duties of officers in other branches of the service. He must be responsible for those under his command and must be entirely capable of meeting any situation that confronts such personnel as is under his direct supervision whether it be in open field duty requiring the setting up of field hospitals or the maintenance of food supply and shelter for his personnel as well as a correlation of the activities of his group with the other services under the same command.

Q Is it true that the armed forces are not making efficient use of their medical personnel?

A There have been many occasions in the past when appearances would lead one to believe that they were not. At the present time efficient use is being made of such personnel and it must always be remembered in this connection that a reserve supply of such personnel must be maintained for immediate assignment to duty. Such a group must have been trained together to meet the situations that it will face immediately after assignment and cannot be gathered together at the last minute to be assigned to some specific post.

Furthermore, the planning of any military campaign requires a complete line-up of all services. If reverses are suffered such men who are held in preparation of projected positions may not be able to fill such positions and must be held for further plans. War, by its very nature, is not essentially efficient, but the lack of medical personnel in the various branches of the armed forces has resulted in a high increase in their efficient use.

Q On the basis of present ratios of physicians to total personnel, which service has the greatest need at the present time?

A The Army ratio is slightly over 5 per 1000, whereas the Navy is somewhat under 4 per 1000. Therefore, the Navy needs men somewhat more than the Army.

Q Why is any man under thirty-eight ever classified as essential?

A He is only essential if he were to leave his community or his institution and there were no replacement for him. No man under thirty-eight is, as a general rule, considered permanently essential, but only essential until he can be replaced by another physician who is not eligible for service with the armed forces.

Q Has not the civilian population been endangered by the number of physicians who have entered the armed forces?

A Not for the Nation at large. There are various problems of redistribution that have been partially or completely solved and some that will be difficult to solve, but if such distribution is equitable there is no shortage at present for minimal adequate civilian care.

Q Will not the needs of the services continue and require that additional personnel leave civilian life?

A To some extent, this is true, but primarily the services will be able to meet their own needs for replacement from the students they are training at present. The Navy may need some additional personnel even though they are also training students. The Public Health Service will continue to have needs since they do not have any students in training.

Q Why do not the armed forces adopt the liberalization of qualifications that exist in England and elsewhere?

A Because it is essential that American standards be maintained for the men in the armed forces as well as on the home front. Comparisons with the armed forces of other nations are not in order any more than comparisons of physician-population ratios on the home front are with those of other nations. The mortality in the armed forces at the present time is astoundingly low and every effort will be made to keep it at that level. This will obviously require further sacrifices on the part of those on the home front, but the Procurement and Assignment Service is constantly aware of the fact that supplies of all kinds must continue to flow to those who are on active duty and that the health of the home front is therefore as much a part of the war effort as is the health of the soldier.

Q. What action does Selective Service take on physicians?

A. Although local boards differ somewhat in their actions, in general, no action is taken at present on physicians or others over thirty-eight. Reclassification of those under thirty-eight is going on constantly and dependency is not considered to the same extent as it was in the past.

Dr. Barton, before the close of the meeting, again stated that the reviewing committee of which he was a member would meet for about ten consecutive days at the Boston Medical Library and was anxious to help all physicians seeking enlistment.

BOOK REVIEW

Diagnosis of Uterine Cancer by the Vaginal Smear. By George N. Papanicolaou, M.D., Ph.D., and Herbert F. Traut, M.D. 4°, cloth, 46 pp., with 11 color plates. New York: The Commonwealth Fund, 1943. \$5.00.

In this well-written and beautifully illustrated atlas, the authors have elaborated another method of making the diagnosis of early carcinoma of the uterus and lower genital tract. Virchow believed that the only absolute means of knowing whether a tissue was malignant was by demonstrating its invasion of other surrounding structures. This view was accepted until recent times, when the diagnosis of cancer in its preinvasive stage was accepted. The study of the cells desquamated from the superficial layers of the malignant neoplasms of the uterus and found in the vaginal secretions, makes, in the hands of those so trained, such a diagnosis possible—that is, the recognition of cancer in areas removed from its origin.

The preparation of the vaginal smear and its staining are taken up in the first chapter, whereas the general classification of the epithelial cells of the vagina and cervix found in the vaginal fluid makes up the subject matter of the second chapter. Six pages are devoted to the cellular contents of the vaginal fluid at different periods of the normal sex cycle, and an equal number of pages to the effect of modified physiologic and of pathologic conditions of the cellular elements of the vaginal fluid. The characteristics of vaginal smears in cancer of the cervix, adenoma malignum of the cervix and adenocarcinoma of the cervix are freely discussed. The characteristics of vaginal smears in cancer of the uterine fundus, adenoma malignum of the uterine fundus and adenoacanthoma of the uterine fundus form the subject matter of an entire chapter. The narrative part of the book is closed by a discussion of the use of the vaginal smear as a diagnostic procedure.

There follow eleven plates showing the various types of cells found in the smears under physiologic and pathologic conditions, with clear and understandable legends. The preparation of these plates must have involved a tremendous amount of painstaking work. The authors offer this method, which, in their hands, has proved to be helpful in the diagnosis of early cancer of the uterus, but they do not advocate it at the exclusion of all others that have given satisfactory results.

The student of uterine cancer, whether working in the laboratory or in the operating room, will find this book a distinct addition to his library.

(Notices on page x)

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CERVICAL-CORD INJURIES*

A Study of 101 Cases

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BOSTON

EVERY discussion of any level of spinal cord injury should be based on two fundamental concepts. These are that spinal cord injuries are different from spinal column injuries without cord involvement, and that all significant spinal-cord injuries are accompanied by spinal shock and its effects. One has only to refer to the literature to discover many authors who draw conclusions concerning the diagnosis, treatment and prognosis of a neurologic injury from a mixed series of both cord and vertebral injury cases. Wegner and I¹ drew attention to this in 1939 in relation to a study we made at that time of the bone lesions accompanying cervical spinal cord injuries. When a spinal cord injury is present, any associated bone injury is secondary and of relatively little importance. Under such circumstances, diagnosis, therapy and prognosis are all primarily problems of the cord injury, and the bone damage is from every point of view, subordinate. Only when there is a back or neck injury in which the spinal cord has been undamaged do the bony structures and any changes in them properly assume first place in the consideration of the case. Until this is generally recognized and acted on but little improvement can be expected in the functional end results of spinal cord injuries.

This report deals only with acute injuries to that part of the spinal cord that is enclosed within the seven cervical vertebrae. As a necessary part of the study, however, consideration has also been given to any associated bony and ligamentous damage done to the cervical spine. There are 101 cases in this series. Fifty-five patients survived, and 47 of these have been followed to an end result for periods varying from six months to fifteen years. Forty-six died, a mortality of 46

per cent. Autopsies were obtained and the cords studied in 17 cases.

Spinal Shock

Spinal shock is a constant accompaniment of significant spinal cord injuries. It is recognized by its effects and is known to occur at once after the infliction of the injury and to last for periods varying from a few hours to months. It has nothing to do with surgical shock. As the result of its presence, all reflex activity below the level of the injury becomes chaotic, unpredictably variable and devoid of any diagnostic or prognostic significance. The deleterious effect of spinal shock is greatest on those reflexes mediated by the spinal segments immediately below the level of injury and decreases proportionately as lower segments are reached. As the location of the injury descends, bladder difficulties and bedsores, for example, become increasingly common because of the closer approximation of the segments controlling these reflexes to the level of injury.

Nature of the Accident

The commonest cause of a cervical-cord injury in this series was by all odds a fall, usually on stairs. Fifty or nearly half of the patients were injured by a fall, in 34 cases on stairs (Table 1). Twenty-four of them died. The next commonest cause was diving, with 8 cases. Only 2 of these patients died. It was not possible to learn the nature of the accident in 16 cases, in 12 of which the patients died. Alcohol is evidently a factor in the production of this kind of injury. Acute alcoholism was present in 23 cases and was almost three times as common in the fatal accidents (17 cases) as in the nonfatal (6 cases). In 15 cases it was associated with the fall that caused the injury. In the other 8 cases the kind of accident could not be determined because of its presence.

*From the Department of Neurosurgery, Boston City Hospital. Presented at the annual meeting of the Massachusetts Medical Society on May 25, 1943.

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Bony and Ligamentous Injuries

Although bony and ligamentous injuries are of less importance than cord injuries, it is more

TABLE 1. Causes of Cervical-Cord Injury.

NATURE OF ACCIDENT	TOTAL PATIENTS	LIVING PATIENTS	DEATHS	PATIENTS WITH ASSOCIATED CEREBRO-SPINAL INJURY
Fall				
On stairs	34	17	17	6
Otherwise	16	9	7	2
Diving accident	8	6	2	1
Automobile accident	9	6	3	2
Struck on head	5	4	1	2
Stab wound	2	2	0	0
Machine shop injury	2	0	2	1
Struck by streetcar	2	1	1	0
Struck by train	1	0	1	1
Athletic injury.				
Football	1	1	0	1
Wrestling	1	1	0	0
Ice hockey	1	1	0	1
Accidental burial	1	1	0	0
Assault	1	1	0	0
Recurrent dislocation	1	1	0	0
Cause unknown	16	4	12	2
Associated alcoholism	23	6	17	

convenient to deal with them first (Table 2). It is apparent that the commonest injury to the cervical spine is one that involves multiple vertebrae. An analysis of the 36 cases of multiple injury shows that 26 centered about the fifth vertebra and 2 others included it. Nineteen patients recovered and 17 died. More than half these injuries caused a dislocation as well as a fracture

determined it proved to be centered around the fifth and sixth cervical vertebrae, with the greater number involving the fifth.

Forty-four cases with bone injury had an associated dislocation and in all but 1 case the dislocation was anterior (Fig. 1). It is probable that with the exception of the first and second vertebrae a true posterior dislocation of the cervical vertebrae (Fig. 2) almost never occurs, and then only rarely in an acute form. This group includes one such case. The patient was struck on the forehead, his head was driven backward, the odontoid was broken, and a posterior dislocation of the skull and atlas on the axis was produced. Fortunately the dislocation was not lethal. Despite its rarity a diagnosis of posterior dislocation is frequently made by x-ray. In this case the mobilized part of the column moved backward in relation to the immobilized part. In the common anterior dislocation the mobilized part of the column moves forward in relation to the immobilized part. If all other factors are omitted, the presence of a dislocation in addition to a fracture increases the chance of death slightly, the mortality being 52 per cent in this group as opposed to 44 per cent in the non-dislocation group.

The ligamentous cases deserve special emphasis. It has been shown that it is possible and must be fairly common for adjacent cervical vertebrae to be dislocated either partially or completely

TABLE 2. Location of Injury and Outcome.

DIAGNOSIS	OUTCOME OF CASE	INVOLVED VERTEBRAS								X-RAY EXAMINATION		TOTAL	
		1	2	3	4	5	6	7	MUL- TI- PLE	UN- DETER- MINED	NONE		NEGATIVE FOR FRACTURE
Ligamentous injury with dislocation	Living						4	2		5		11	11
	Dead						0	0		0			0
Fracture with dislocation	Living	1			0	4	4	1	11				21
	Dead	0			3	6	3	1	10				23
Fracture only	Living			1		7	2	1	8				19
	Dead			1	1	2	5	0	7				16
Stab wound	Living					2							2
	Dead					0							0
Acute rupture of intervertebral disk	Living				1								1
	Dead				0								0
Type of injury undetermined	Living										1		1
	Dead										7		7
Totals		1	0	2	5	21	18	5	36	5	8	11	101

of the involved vertebrae. In the single fractures, whether with or without dislocation, the same preponderance of location appears, 21 involving the fifth and 18 the sixth vertebra. Moreover, in the one patient who had a rupture of a cervical intervertebral disk with an immediate and acute extrusion of the nucleus pulposus, the involved disk was that which separated the fourth and fifth vertebrae. Thus in 60 of the 93 patients in whom the site of the bone injury was certainly

without bone injury and by virtue of a tearing of the capsular and other ligaments that surround the articular facets.¹ This series includes 11 such patients, none of whom had any demonstrable injury of the vertebral column. The cord injuries included among other diagnoses classic cervical hematomyelia and transection. This has convinced me that it is possible for cervical vertebrae to be momentarily dislocated sufficiently far to damage the cervical cord, even to the point

of transection, only to return to apparent normality long before the physician sees the patient. None of these 11 patients died. The location of the injury as evidenced by the segmental level of the symptoms was again concentrated around the

tion or sufficient clinical observation to be unmistakable in 68 of the 101 cases.

There were 13 transections. All the patients died except 2, who were living six months and three years, respectively, after the accident. In one case the transection developed ten days after injury. In this interval a diagnosis of mild contusion had been made and was thought to have been confirmed by operation. The transection developed suddenly and is believed to have been



FIGURE 1. *Anterior Dislocation of Cervical Spine (lateral view).*

fifth cervical vertebra, with a tendency to move downward, particularly in the transected cases. As has been pointed out,¹ it is these injuries that are apt not to unite until late, because healing depends solely on ligamentous repair.

One should not jump to the conclusion from these figures that the preponderance of acute cervical vertebral injuries involve the fifth vertebra. Indeed, it can be easily demonstrated that they do not. The present figures apply only to the patients with acute cervical cord injuries. A realization that any significant acute injury to the cervical cord at or above the fourth cervical segment produces complete respiratory paralysis will explain why cases of damage to the higher cervical vertebrae were so rare in this series. Either the patient was dead before arrival at the hospital and was taken directly to the morgue or was not suffering from involvement of the cord as the result of the accident.

Pathology of Cord Injuries

The pathologic changes produced in the cord by the injury were confirmed by autopsy, opera-



FIGURE 2. *Posterior Dislocation of Lumbar Spine (lateral view).*

caused by interference with the cord circulation locally, resulting in something of the nature of a thrombomyelitis. Respiration was entirely diaphragmatic, and what little motion remained in the arms and shoulders was entirely useless. Of the remaining 11 cases the diagnosis was confirmed clinically in 2, by operation in 1, and by autopsy in 8. In all, the damage lay between the fifth and eighth cervical segments.

There were 6 contusions of the cord. Two were verified by operation, 2 by clinical observation.

and 2 at autopsy. Only 1 patient survived. Six cases originally diagnosed clinically as contusion proved to have transections at autopsy (5 cases) or at operation (1 case). No patient originally diagnosed as having contusion was discharged with that diagnosis. There were 6 cases with pure compression of the cord, without other myelogenous damage. Two patients survived, with clinical confirmation in one case and operative confirmation in the other. In the 4 fatal cases, the diagnosis was confirmed by operation in 2 and by autopsy in 2. The presence of edema of the cord was never confirmed by either operation or autopsy. There were 5 cases in which the clinical findings justified this diagnosis. All except one of the patients survived.

The commonest pathologic condition was hematomyelia, with or without edema. It is possible that some of the surviving cases classed as hematomyelia actually had a mild contusion. Short of microscopic examination such a differentiation is impossible. Because the symptoms and course were analogous to those of proved cases of hematomyelia, however, they have been classified in the latter group. There were 35 of these cases. Twenty-nine were confirmed clinically, 3 by operation, and 3 by autopsy. Twenty-six patients survived.

Two cases of stab wounds and 1 of radiculitis were confirmed clinically, and all the patients survived. In 3 cases the diagnosis was not certainly known and in 30 it could not be verified. Because the cord lesion has necessarily to be located below the fourth segment if a patient with any significant acute cervical-cord injury is to live long enough to be hospitalized before he dies of respiratory failure, and because the area of cervical cord below this point is so small that an estimate of the differential effects of injury at different segmental levels within this region is impossible, no effort has been made to study the distribution of the cord injury in more detail.

Diagnosis

It seems certain that the best one can do in making a diagnosis at or close to the time of the sustaining of a cord injury is to determine the approximate upper level of the damage by a sensory examination. Except for this information the doctor is limited to the decision whether the lesion is of the type that causes a block of the flow of the cerebrospinal fluid. The lesions that cause such a block are edema, with or without hematomyelia, contusion, compression and concussion of the cord. The compression may be caused by a meningeal clot, a fragment of fractured bone, the crushing of a vertebral body, a dislocation of a vertebra or an extrusion of a nucleus pulposus. Contusion is self-explanatory and may be com-

bined with compression. Concussion is associated only with bullet wounds of the bony wall of the canal. The lesions that do not cause a block of the flow of the cerebrospinal fluid are hematomyelia without edema, anatomical transection and rarely an overlapping tear in the dura and arachnoid with an undetermined amount of cord injury. This last permits cerebrospinal fluid to be diverted to the extradural or subdural space and thus prevents filling of the subarachnoid space below the point of injury. Such findings may lead to the diagnosis of cerebrospinal-fluid block when none is actually present. Conditions that produce no block may be present as a complication of any of those that do cause a block and, of course, be unrecognizable, but the reverse is never true. Final differentiation between pathologic entities within these two classifications must await the final outcome of the case and may not be possible for months or even years. Even then it may be impossible unless major sepsis is not present, the patient is not suffering from hypoproteinemia, the bladder has reached a satisfactory functional end point, and proper physiotherapy and splinting have been practiced.

Disagreement between the immediate and final diagnoses is common in all cord injuries. Even observations made of the exposed cord at operation are not necessarily accurate or dependable. This is particularly true when the cord looks as though it had sustained little or no damage so far as its surface goes. Because the vascular supply to the cord is minimal and so constructed as to produce a bottleneck^{2,3} in both the arterial and venous channels, its tissue is particularly vulnerable should damage to the arteries or venous thrombosis occur. Cells that would not have sustained lethal damage in any other tissues do not recover, and a spreading myelomalacia may develop in the presence of damage to a single artery or of thrombosis of a single vein at certain levels on account of the lack of collateral circulation. A detailed study of this series has demonstrated that in 32 cases the immediate and final diagnoses agreed and in 36 they did not agree. Whether there was agreement or disagreement could not be determined in 33 cases (Table 3). Agreement and disagreement were determined by autopsy, by operation provided the patient lived more than forty-eight hours or by clinical observation provided he lived one year or longer after the accident. The immediate diagnosis was that made as soon after the accident as adequate studies had been completed. Under these conditions agreement was held to be present in 3 cases of transection, 22 cases of hematomyelia, 3 cases of compression without other pathology, 1 case of edema, 2 cases of stab wounds and 1 case of radiculitis

A preliminary diagnosis of contusion of the cord was never verified. Thus, only 28 of 54 cases were correctly diagnosed when first seen. Only 1 of the 11 diagnoses made at operation was confirmed

In the light of this evidence it cannot any longer be seriously contended that either the rapidity of onset or the amount of paralysis following an injury to the cervical levels of the spinal cord is of

TABLE 3. *Difference between Immediate and Final Diagnoses.*

IMMEDIATE DIAGNOSIS	TOTAL NO OF CASES	DIAGNOSIS CONFIRMED	DIAGNOSIS ALTERED					FINAL DIAGNOSIS		
			TRANSEC- TION	CONTU- SION	COMPRES- SION	EDEMA	HEMATO- MYELIA	LIVING PATIENTS	DEATHS	TOTAL NO OF CASES
Transaction	4	3					1	2	11	13
Contusion	10	0	6	2			2	1	5	6
Compression	14	3	3	3			5	2	4	6
Edema	8	1	1		1		5	5	0	5
Hematomyelia	28	22		2		4		26	9	35
Sub wound	2	2						2	0	2
Radiculitis	1	1						1	0	1
Fractured spine	1	0		1				0	0	0
Totals	68	32	10	6	3	4	13	39	29	68
Not made										33
Grand total										101

later. This was in a case of compression. Of those cases in which the two diagnoses did not agree the patient's condition was worse at discharge than it was at admission in 26 cases.

In summary, it seems reasonable to conclude that a diagnosis of hematomyelia is the most apt to be correct, and if wrong is least liable to turn out to be something more serious. On the other hand, contusion, compression and edema are the conditions least apt to be correctly diagnosed and the most likely to be finally diagnosed as a condition that is much more serious than the original one was thought to be. This last is true not so much because of inaccuracies at the time the first observations are made as because of the progressive disintegration in the cord tissue that goes with compression of the cord. This compression may come from within and be traceable to edema, large hemorrhages or the results of altered circulation, or from without because of the effect of bone fragments, meningeal clots and the like. This fact has its practical aspect in that it points to the desirability of relieving extraneous pressure as early as possible, and at the same time emphasizes the danger attendant on operative procedures that are carried out in the face of a cord already damaged by edema or by hemorrhage within its substance. In particular it indicates the folly of splitting the cord and thus running the risk of producing damage that might not otherwise occur.

Diagnostic and prognostic conclusions based on the onset, type and extent of motor and reflex disability are never justified. Recognition of this fact is extremely important. It comes about because of the changes wrought by spinal shock. Fifty-five of the patients in this series could be studied in detail from this point of view (Table 4).

any diagnostic or prognostic significance whatsoever.

The demonstration of the presence or absence of a block of the flow of cerebrospinal fluid is made by a study of the total protein content of the fluid

TABLE 4. *Onset and Type of Paralysis.*

DIAGNOSIS	TOTAL NO OF CASES	ONSET		TYPE	
		IMME- DIATE	DE- LAYED	COM- PLETE	PAR- TIAL
Transaction	10	6	4	3	3
Contusion	5	1	4	0	1
Compression	5	2	3	2	0
Edema	4	0	4		
Hematomyelia	27	17	10	8	9
Sub wound	2	1	1	0	1
Radiculitis	2	1	1		
Totals	55	28	27	13	15

below the block and the performance of a fractional Queckenstedt test. Evidence of block consisting in an increase in total protein frequently appears before the evidence of dynamic block, and always outlasts it. The fractional Queckenstedt test is best done by compressing the jugular veins, not by hand but by inflation and deflation of a blood-pressure cuff wrapped around the patient's neck. Observations on the intraspinal pressure are made and recorded with every 10 mm. increase of pressure in the cuff from 0 to 40 and similarly with every 10 mm. decrease from 40 to 0. Partial dynamic blocks are recognizable by this method when every other has failed. As has been pointed out above, if a block is present, the patient is suffering from either edema, with or without hematomyelia, contusion, compression or concussion of the cord. If a block is absent, he is suffering from either hematomyelia without edema or an anatomical transection. The only source of diag-

nostic error lies in the rare possibility of the patient's having coincidental tears in the dura and arachnoid and presenting signs that superficially appear to indicate a block when there is actually none present. Further diagnostic differentiation is unjustified and impossible until the lesion has reached an end point.

Nonoperative Treatment

Certain general principles of treatment must be adhered to if the end results that the patient has a

other method that aims to accomplish rapid hyperextension are also contraindicated. Sufficient protein must be given in the diet or by transfusions or other means to maintain the serum protein at 6.0 gm. per 100 cc. or better. The salt intake must usually be increased also, and the patient should be started at once on large amounts of all the vitamins. While he remains on tidal drainage the fluid intake should never be allowed to fall below 4000 cc. per twenty-four hours for an adult with a normal cardiorenal system. Care

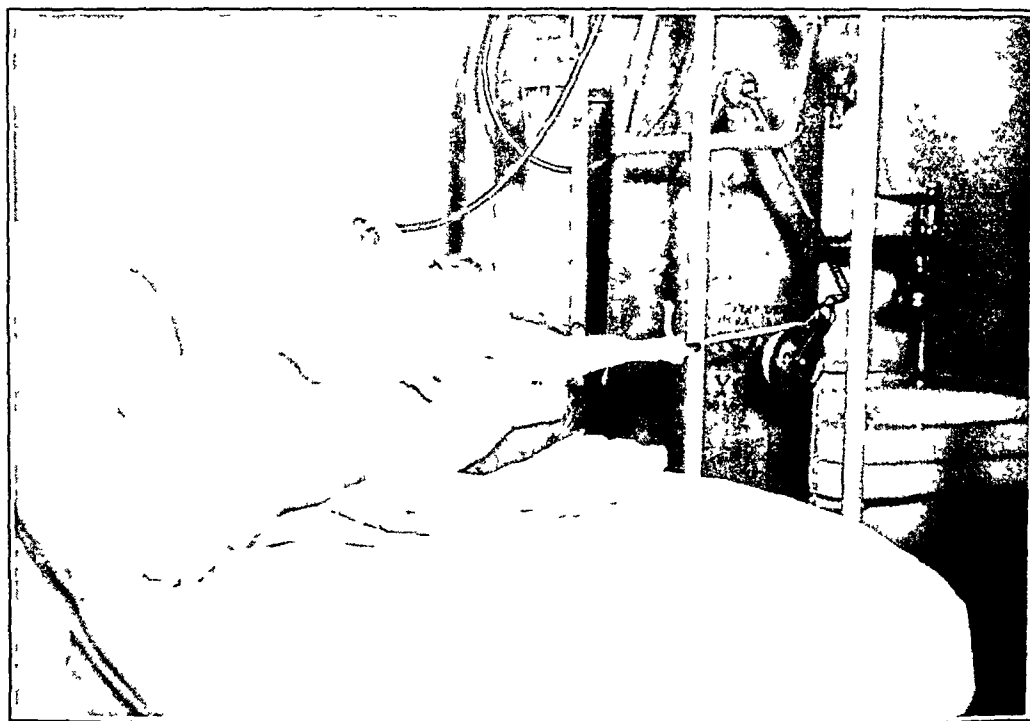


FIGURE 3. *Bridle Made from Folded Flannel Bandages.*

right to expect are to be obtained. In every case of spinal-cord injury the bladder should be emptied and an inlying catheter fastened in place at the earliest possible moment. As soon afterward as it can be done this catheter should be attached to a tidal-drainage apparatus properly adjusted by cystometry to the needs of the bladder. Simultaneously the patient should be treated for surgical shock if and when it is present. Both steps should precede all but the most superficial diagnostic measures. The demonstration of the presence or absence of a block should always follow the above and come before all other measures. Splints, no matter what their material, that are fixed in relation to the patient must never be used in spinal-cord injuries, especially in thoracic and lumbosacral ones. In particular the application of plaster of Paris is contraindicated regardless of the amount of padding used. So, too, are rubber and other rings or doughnuts, Bradford or other frames and water or air mattresses. Metal frames and any

must be taken to keep the bowels open and prevent the development of fecal impactions. All patients must be moved off the back and onto one or the other side every two hours, day and night, during their stay in bed. They should never be allowed to lie in a wet bed for even as little time as fifteen minutes. These are general measures that apply to all patients with spinal-cord injuries until such time as anatomical and functional end results have been reached, regardless of the diagnosis. Other procedures depend on the presence or absence of a positive Queckenstedt test. This reaction must be determined in every case without exception, and the test should be made after the patient is out of surgical shock and on tidal drainage.

It is vitally important in all patients with cervical-cord injuries that the head be not accidentally flexed. This control of the movements of the head on the spine is equally essential whether or not there is a cerebrospinal fluid block. It is

best accomplished by traction of the head in extension with a bridle. It can be achieved by the application of some form of fixed splint, such as a Thomas collar or a plaster cuirasse, with or without a jury mast, but my experience has shown

In general and unless there is some special indication, traction in all cases of cervical cord injury should be parallel to the long axis of that part of the cervical spine that has not been dislocated or moved. Under such circumstances it is

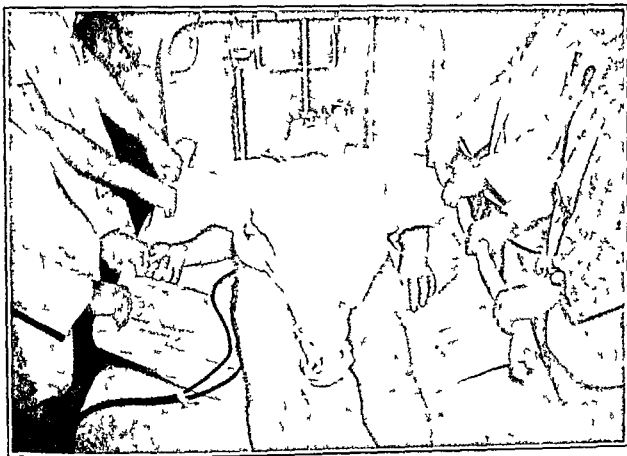


FIGURE 4 Moving a Patient in Bed with the Aid of a Drawsheet
Note the sheet stretched tightly beneath the patient

that these applications can do no more than traction does, usually do not do so much, and are much more difficult and dangerous to use. Under the circumstances the best apparatus is the one that is simplest and easiest to apply. As can be seen in Figure 3, such an apparatus can be made from two flannel bandages each folded lengthwise a number of times until an appropriate length is reached. One of these bandages is looped around the chin and its free end attached to a spreader, which in its turn has a piece of rope hung from its center point. This rope passes over the pulley of an ordinary Buck's extension apparatus that is attached to the bed, and terminates in a loop that supports a 5 pound weight. The other bandage is looped about the occiput and the free ends are pinned to those parts of the first bandage that are opposite the ears. The head of the bed should be slightly elevated. By adjusting the relative lengths of the bandage loops and the height of the pulley in relation to the line of pull, traction can be exerted on the head with simultaneous control of the flexion and extension of the neck. Commercial bridles have no advantage and offer many disadvantages compared with this simpler one.

well to put a soft pillow under the head. If extension is required, a small hard pillow should be put under the shoulders. I have not used tongs but have used piano wire looped through adjoining trephines on either side of the vertex of the skull as a means of applying traction and using greater weights than are possible with the flannel bandage bridle. I have been unable to accomplish anything more by this method than I was able to do with the bridle. Regardless of the weight applied, all that traction can do is to stretch the muscles and ligaments of the neck and tire out the former. The constant application of 5 pounds of traction will accomplish this as expeditiously and as efficiently as will a heavier weight. Neither method nor any amount of weight will relocate a locked dislocation without accompanying and proper adjustment of the line of traction. When this is provided, 5 pounds of traction will move the articulating facets as efficiently and more accurately than greater weights. This has been described in detail elsewhere.¹

If a block is absent there is no need for operation, and x-ray films should be postponed until they can be taken without risk to the patient.

The patient should be placed on an

way. This brings a wide linen drawsheet beneath the buttocks and back (Fig. 4). It is this drawsheet that should be used to turn the patient at the end of every two-hour period. With an ordinary adult it requires at least three and better

The patient's feet should be supported at right angles, with the bedclothes held off them by a cradle, and the knees should be supported on pillows in slight flexion. Particular pains should be taken to see that the paralyzed hands and arms are



FIGURE 5. *Moving a Patient in Bed with the Aid of a Drawsheet.*

The patient is partially turned toward his left side. Note that the patient's head is rotated simultaneously.

five persons to do this. Each of the lateral edges of the drawsheet is grasped by one or two nurses and the sheet is pulled tight underneath the patient. Another nurse holds the patient's head face-up between her hands (Fig. 5). If the patient is to be turned from his back to his left side, the nurse or nurses holding the drawsheet edge to the right of the patient, bring it upward and toward the other side of the bed until it is in contact with the patient's back and side. The drawsheet is kept stretched tightly at all times. A continuation of the movement rolls the patient onto his left side. Simultaneously the nurse holding the patient's head turns the latter in concert with the body (Fig. 6). Once the rotation is accomplished, the drawsheet is used to lift and move the patient back to the middle of the bed (Fig. 7). The traction is not disturbed. To move the patient from his side to his back the sheet is brought to the last position described above, and with this as a starting point the rest of the process is done in reverse. Every patient with any kind of spinal-cord injury can be moved safely as often as need be by this method. It is much safer and more efficient than the use of Bradford frames or any similar apparatus.

not allowed to get into awkward or strained positions or to get beneath the body. They should also be kept off the chest and particularly the abdomen — not because of damage to the extremities but because their dead weight will seriously impede respiration. This is especially dangerous and may make the difference between life and death during the early period after the injury when respiration is either wholly or mostly diaphragmatic. Physiotherapy should be begun and maintained as long as the patient's muscles are not hypertonic. If they are, it is harmful and contraindicated. The latter situation, however, scarcely ever arises in cervical-cord injuries. When it does occur, it is usually a late manifestation of transection of the cord.

Care of the hands is particularly important in all these cases. In many it is also particularly difficult. This is especially true in alcoholic patients or others who have had an inadequate diet, in manual laborers and in patients over fifty years of age. In many of these patients the small muscles of the hand atrophy early, a general swelling of the subcutaneous tissues of the palm and back of the hand and the areas around the finger joints takes place, and stiffness and immobility of the

joints, and in some cases intra-articular adhesions, develop. These changes reach their maximum height in about three weeks after the injury. They make their appearance and persist in spite of adequate and early physiotherapy, although with

Three patients with the above signs, two of whom were alcoholic, over fifty five, manual laborers and suffering from hematomyelia, and who had had advanced and uncorrectable disability of this type for seven and three months respectively.

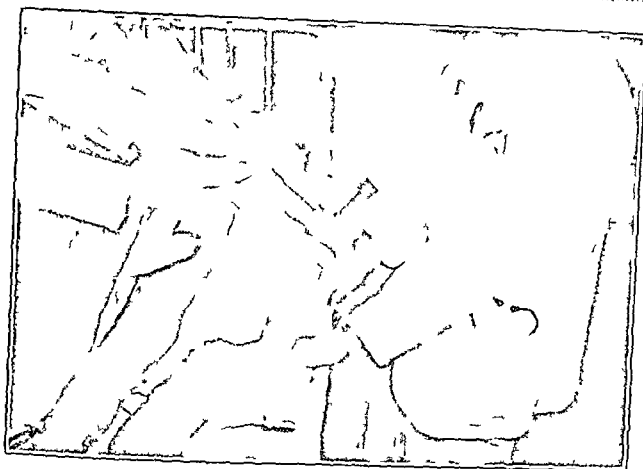


FIGURE 6 Moving a Patient in Bed with the Aid of a Drawsheet
The patient has been turned so that he lies on his left side

out if they appear earlier and are worse. The hands have a characteristic flat appearance and are best described by the appellation "flippers." As a result, although innervation of these small muscles is complete at the usual time and in accordance with the amount and degree of recovery from the cord injury, function fails to return—perhaps permanently—because of the soft tissue swelling and the immobility of the joints.

Because of my belief that this might be an arthritis problem, Dr Francis C Hall was asked to see certain patients suffering from this condition. It was his opinion that the lesion was neither arthritic nor periarthritic in the usual sense of the word. He suggested that it had its origin in a combination of subclinical avitaminosis and impairment of the circulation in the upper extremities. For the avitaminosis he suggested the following: eight yeast tablets or one teaspoonful of Vegex three times a day, 3 cc of crude liver extract twice a week, one tablet of Lederle's vitamin B complex every hour for twelve doses daily for two to three weeks and the avoidance of catharsis when possible. For the circulatory deficiency he suggested diathermy three times a week through the back over the origins of the brachial arteries.

were put on the above regime. The third patient was nonalcoholic, over sixty, a foreman, and was suffering from a cervicodorsal transection, he had had the same disability for three months but to a lesser degree than the others. Within a month the hands of all these patients had regained their normal appearance except for the atrophy of the small muscles, the swelling was completely gone, the local circulation was noticeably improved, and the mobility of the joints and consequent usefulness of the fingers had increased by 30 to 50 per cent. During this time every application of the diathermy had caused pain in the shoulders and down the arms. Since then the improvement has continued, but more slowly, and this pain has disappeared. One other patient—a woman of forty eight, alcoholic and a manual laborer with a hematomyelia—was treated in this way from the start. Four months after injury she had had no more than the expected trouble in regaining the usefulness of her hands and had never shown any of the signs listed above, although she was believed from the start to be a patient who under other circumstances would have certainly developed disability from this cause. Although many more observations must be made and many more of such patients seen

and studied before even tentative conclusions can be reached, the experience seems sufficiently striking so that the profession at large should have the benefit of it.

At the end of six weeks in a case in which there has been bone injury and there is adequate evi-

I have never seen any harm done by too prolonged splinting in cases of cervical-cord injury, but have seen unnecessary invalidism develop because of too short a period of both traction and splinting.

The problems inherent in transection of the cord arise only infrequently in cervical-cord in-



FIGURE 7. *Moving a Patient in Bed with the Aid of a Drawsheet.*
The patient is moved back to the center of the bed.

dence of repair by x-ray, or after eight weeks in those in which there has been minimal or no evidence of bone injury, the patients can be allowed out of bed after being fitted with a modified Zimmer brace (Fig. 8).⁴ Elderly patients can be allowed out of bed as early as two weeks after the injury if their general condition warrants it and they wear one of these braces. This practice is justifiable only under special circumstances, however, and should not be applied as a general rule. By the end of six or eight weeks and usually earlier, those patients who have had hematomyelia regain normal control of the bladder and bowels. Constant x-ray check should be made of their bone injury until such time as the physician is certain that it is completely healed. The splint should be worn constantly during this period. This is doubly important if the injury has been ligamentous. Check by x-ray for redislocation in such cases should be frequent and should be continued for four months after the splint has been removed. Evidence that redislocation is developing necessitates the return of the patient to traction in bed and more prolonged splinting. Practically all patients with transected

cervical cords die within the first week after their injury. This is particularly true with complete transections. I have never seen a patient with a complete cervical transection develop a mass reflex. As a result, tidal drainage has been adequate and efficient in the care of their bladders. The 2 patients with partial transections who have survived for a longer period have flexion and adductor spasm but none of the excessive motor response to minimal sensory stimuli that characterize the next stage in complete transections and that are the chief characteristic of the mass reflex. The greatest problem in these cervical transections has been caring for the distention that under other circumstances would do little or no harm. In these patients respiration is entirely diaphragmatic. The increased intra-abdominal pressure inherent in distention splints the diaphragm, with a resultant decrease in respiratory efficiency, the development of pulmonary disease and death. Avoidance of fluids, including water, by mouth for the first three to five days and the use of rectal tubes, milk and molasses enemas, physostigmine and similar drugs and procedures, repeated frequently or used constantly, are the best means of

combating this condition. Abdominal operation is contraindicated and will kill the patient if performed.

Operative Treatment

In patients who have a positive Queckenstedt test the question arises whether this block should

be relieved, regardless of the symptoms and signs of block. During this period the surgeon must depend on properly adjusted traction and improvement in the oxygenation of the tissues to reduce to a minimum any permanent damage to the cord. If at the end of this time a complete block is still present or a partial one is increasing and the pa-

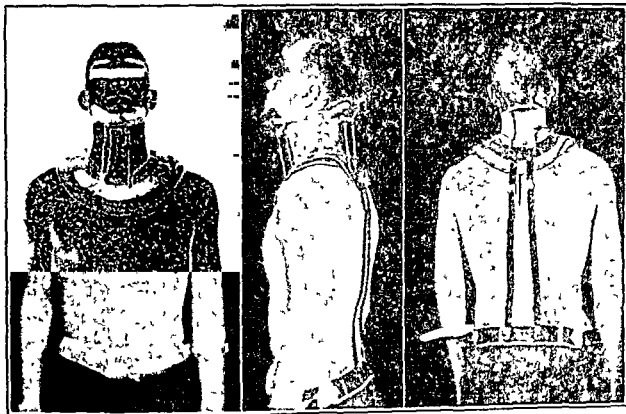


FIGURE 8. *The Modified Zimmer Brace*

be relieved by a decompressive laminectomy, and if so how soon after the injury. This procedure is not to be undertaken lightly. A comparative study of two similar groups of cervical-cord injuries demonstrated that in 30 patients 43 per cent of whom were operated on, the mortality was 63 per cent, whereas in 46 patients 15 per cent of whom were operated on it was only 33 per cent. In other words, when the number of decompressive laminectomies was reduced by 28 per cent the mortality was reduced by 30 per cent. All these patients are included in the present series. A study of the lesion, as noted above, points in the same direction. Those conditions (contusion, edema and compression of the cord) that at first sight are most in need of early decompression are the ones that end, whether operated on or not, with transection or at least a more serious pathologic condition than was originally believed to have been present. Operation therefore can only do harm unless it is postponed until the changes produced in the cord by the injury have become stabilized. This does not mean that other methods of treatment should be abandoned during this period, nor does it mean that decompression may not prove helpful after the period has passed. It does mean that operative decompression during the first five to seven days after the injury is not

justified, regardless of the symptoms and signs of block. It should be extensive enough to free the block completely and the operation should be limited to this procedure only.

I am strongly opposed in these cases of cervical cord injury to any attempt to manipulate the damaged bones as part of the operative procedure. The cord has been sufficiently endangered already without adding the chance of injury from a slipped instrument, a loose fragment that had not been seen or a redislocation during closure because of an unrecognized partial reduction. Any necessary and possible change in the bony alignment can be better accomplished by properly applied traction. I am opposed also to the use of silver wire or other material for the purpose of tying one spinous process to another in the belief that this will control the movements of the damaged vertebra or vertebrae. Any control comes from proper reduction and sufficient splinting, and in spite of and not because of a loop of wire. Furthermore, the presence of wire is not necessarily innocuous. I have removed one that was surrounded by dense fibrous tissue continuous with a scar in the canal that deformed the dura the cord and the roots over three segments on one side. The resultant symptoms were disabling.

If possible it is best to use Avertin and local

anesthesia. If the condition of the patient is such as to preclude the use of local anesthesia, Avertin followed by Pentothal Sodium intravenously is the next choice and is preferable to an inhalation anesthetic. Its administration should not be attempted, however, unless a cannula is inserted and tied into an ankle vein and kept open by dripping 5 per cent glucose in salt solution into it. The Pentothal Sodium should be administered by puncturing the rubber tubing of this system close to the cannula with a needle attached to the syringe containing the drug. If the drug is given slowly and repeated often enough, there will be no trouble with the respiration.

Before a final decision can be made as to operability, information relative to the bone condition must be obtained. This should be done as soon as it is known that a block is present. Thus, in blocked cases x-ray examination is essential some time during the first seventy-two hours or as soon thereafter as it is possible and safe to make it. This should include a stereoscopic anteroposterior view and right and left stereoscopic oblique views. A single lateral view can be taken, but one should not expect a great deal from it, especially in the lower cervical injuries. It should never be forgotten that a negative x-ray finding in cervical-cord injuries is more important than a positive one in that it suggests ligamentous rather than bone damage. Bullet wounds and stab wounds are compound injuries and as a general rule should be débrided when it is safe to do so. Whether or not the wound is débrided, however, the sulfonamides should be administered by mouth or intravenously and applied locally to the wound. Beyond this, it is impossible to be more specific. Each case must be settled on its merits, always bearing in mind that the preservation of the patient's life is a necessary prerequisite to his recovery from any paralysis he may have. While the surgeon is reaching a decision as to whether and when to operate, or whenever the block is relieved, the care of the cord injury and the patient is the same as that outlined in the previous section.

Transportation

The problem of how and when to move patients with a cervical spinal-cord injury may arise at any time, and experience in relation to it is particularly apposite in view of the widespread public education in first aid. One fundamental factor governs. This is that the patient's head must under no circumstances be flexed on the chest. Pure extension within reason is harmless, and fixation in mild extension is ideal. Flexion is inexcusable, and denotes complete ignorance of the problem at hand. Patients who walked into

the hospital have been changed into bedridden invalids with paralysis of all four extremities after their necks have been flexed in the course of a clinical examination. In other cases flexing of the neck in the course of moving patients from the scene of the accident to a litter has resulted in instant death. The danger attendant on any flexion or any possibility of flexion of the head on the chest in actual or potential cervical-cord injuries cannot be emphasized too strongly in view of the directions for moving such patients given in the *American Red Cross First Aid Text-Book*⁵ and the sixth volume of *Military Surgical Manuals*, published under the auspices of the National Research Council.⁶ The former is the book used for the instruction of first-aid classes. Specific directions are given there, including a photograph, that a victim with an actual or suspected broken neck must be kept with his face up if lying on his back or turned to a face-up position if lying on his face previous to transportation. This is despite the fact that the directions for caring for a broken back call for transportation in the face-down position unless a combination of broken neck and back is suspected, in which case the victim must be carried with his face up. The latter, a recent publication, is intended for the use of the medical departments of the Army and Navy.

Transportation face up is dangerous for several obvious reasons. Many of these patients vomit. They are paralyzed and cannot move or be moved. When they vomit in this position, the vomitus necessarily gravitates to the back of the throat and is almost certain to be inhaled. This causes atelectasis or pneumonia at best and death by strangulation at worst. Attendants are of no help in preventing such a complication because with the patient in this position they cannot move his head without flexing his neck. This is recognized even by the Red Cross as being extremely dangerous. With the patient in the face-down position this situation can be avoided.

Another source of danger is the self-appointed assistant. He is ubiquitous, and his judgment is as bad as his intentions are good. A request by the patient for a drink of water or a more comfortable pillow, or that his head be moved, or similar suggestions by a bystander, will, if gratified, lead to flexion of the head on the chest when the patient is lying face up. In the face-down position, on the other hand, movement of the head is limited to turning or extension. Either one of these is relatively safe and is therapeutic in comparison to flexion. Many patients with cervical-cord injuries are unco-operative and confused, and persist in trying to get off the stretcher. If they are face up they can and may kill themselves in the course of such attempts, whereas

if they are face down their chances of doing themselves harm are much reduced.

Patients with broken necks who have to be moved before they can be laid face down must have some sort of temporary splint applied to the cervical spine. Such persons are those who are held erect or in a sitting position after the accident or who have to be brought out of a confined space. Among the latter are men injured in tanks or in single seated fighting planes. Attempts to extract these patients without such splinting almost inevitably leads to flexion of the neck and an increase of cord damage as the least serious result, and instant death as the most serious one. Any splint applied to prevent this development must be easily available, and of such a type that it can be wrapped around the neck before the patient is moved. It needs only enough body to give it stiffness for ten or fifteen minutes. A newspaper fulfills these requirements as well as anything else. It should be folded lengthwise in such a way that its width equals the distance between the angle of the lower jaw and the clavicle. It is wrapped around the patient's neck without moving him and held in place with a piece of string. This is a temporary arrangement, and should not be expected to do more than steady the head on the shoulders during the moving. Neither this nor any other kind of splint need be applied to such patients' necks when they are lying face down, and must not be put on when they are lying face up. For the rest, I am in agreement with the recommendations given in the Red Cross manual. They insist that such patients should always be rolled and never lifted, that they be carried on a solid litter or its equivalent that is longer and wider than the patient, and that the neck and head be supported on both sides by the equivalent of sandbags so that the head cannot roll. When the patient is carried face down, one of his arms should be placed in such a position that the forehead rests on the extensor surface of the forearm. To accomplish this the elbow must be bent at right angles and adjusted in such a position that the forearm lies at right angles to the long axis of the body. Unless and until these requirements can be fulfilled, it is much better and infinitely safer to leave the patient where he is, even if this necessitates standing guard over him, redirecting traffic and the like. Certainly these are no cases for amateur handling.

Complications

One of the commonest and usually forgotten or unrecognized complications of cervical spine and cervical-cord injuries is a craniocerebral injury. Nineteen patients in this series, or 19 per

cent, suffered from craniocerebral injuries, and 7 died. The lesion and treatment are no different from those of the craniocerebral injuries that are not complicated by injuries of the cervical spine or cord (Table 1).

Other significant complications of cervical cord injuries are interference with the return of function of the hands and the conditions traceable to impairment of respiration. The former has been discussed sufficiently above. Impairment of respiration is a necessary consequence of practically any cervical cord injury. Either the injury itself or spinal shock will at least reduce and may do away altogether with the usefulness of the costal muscles. As a result, all respiratory exchange must depend for a variable period of time on the diaphragm. This muscle is not equipped to carry such a load unaided and without a chance for adjustment. Respiratory irregularities and deficiency result and may go on to the point where death follows. Distention, restlessness, anoxemia, other injuries, necessary or unnecessary operative procedures and the like all further impede the action of the diaphragm. Unfortunately, the general bodily changes that may be associated with such conditions are not well understood. Treatment is therefore purely empirical and not of great avail. Investigation now going on in my clinic will I hope—eventually settle some of these questions but it has not proceeded far enough to justify any final conclusions. At the moment we believe that in practically all cervical transections at any level and in most of the other more severe injuries that involve the cervical cord close to the fifth segment the diaphragm must provide the motive power for respiratory exchange for a variable period of time—from a few hours up to the rest of the patient's life. During the first week after the injury or until the first effects of spinal shock have worn off, the diaphragm attempts to adjust itself to this unaccustomed load. If this proves impossible, cyanosis, restlessness, an increase in respiratory rate with a decrease in amplitude and signs of fluid or consolidation in the lungs develop. In the later stages confusion and disorientation further complicate the picture, but whether these are caused by anoxemia or something else is not clear. This syndrome is probably traceable to tiring and consequent inefficiency of the diaphragm, with a resultant decrease in respiratory exchange. It usually but not always results in death. In our experience a respirator and other mechanical substitutes for costal breathing are not only of no help but are actually a hindrance because of the impossibility of adjusting the respirator rate to that of the patient. We have not, however, tried paralyzing the patient's respiration entirely and depending on

PURPURA FULMINANS (THE WATERHOUSE-FRIDERICHSEN SYNDROME)

Report of a Case with Recovery

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THE Waterhouse-Friderichsen syndrome — adrenal hemorrhage associated with purpura — is also known as acute hemorrhagic adrenalitis, suprarenal apoplexy and purpura fulminans. Although the clinical picture was first described in 1901, until recently it has been regarded a very rare condition, and one that is rapidly and invariably fatal.¹ The diagnosis is still not often made clinically.^{2,3} Until February, 1943, there were but 103 cases reported in the literature, and among these there were only 3 recoveries.³

With few exceptions the condition is observed in children between the ages of two months and two years. Seventy per cent of all cases fall within this age range, and 90 per cent of all patients are under nine years of age.^{3,4}

The similarity of the course of this disease to that of meningitis and the frequent finding of the meningococcus as the etiologic agent have given rise to a feeling that this is the only cause of the syndrome.³ Actually, although the meningococcus is the most commonly found agent, there are many possible etiologic factors. In newborn infants, trauma and asphyxia of long and difficult labor, hereditary syphilis and maternal eclampsia have been thought to be implicated.¹ In older children and adults, adrenal hemorrhage has been found to occur in the course of many acute infectious diseases, especially scarlet fever, diphtheria, pneumonia and meningococcal meningitis.³

The exact cause of adrenal hemorrhage is not known. Anatomically, the vessels of the adrenal glands are characterized by extremely thin sinusoidal walls in close contact with the parenchyma. It is believed that a toxic effect is exerted on the vessel walls, increasing their permeability and resulting in extravasation of blood.³ Venous thrombosis is also seen, but this is believed to be a secondary effect. The hemorrhage is located chiefly in the medullary portion of the gland and extends into the cortex, mostly by contiguity. Adrenal hemorrhage is bilateral in 95 per cent of cases, and when unilateral the right suprarenal is practically always involved. Grossly the gland may be enlarged in cases of severe hemorrhage, but its contour is usually not changed.¹ Variations in severity of hemorrhage from petechiae to

gross extravasation are directly correlated with the severity of the clinical picture.⁸

Previous to the last few years the clinical picture has not been well recognized,⁴ and the diagnosis has rarely been made before autopsy.^{1,2} Features described by observers reveal that the general picture varies considerably, but after the onset, with actual adrenal damage, the pattern becomes clearer and more typical and should be recognized, or at least suspected, oftener than it has been.

The initial symptoms are the nonspecific ones encountered at the onset of any infectious disease. Malaise, fatigue, headache, digestive disturbances and a slight rise in temperature are common. Frequently there is an accompanying upper-respiratory infection. A more suggestive but less frequently encountered train of symptoms is that which occurs when a previously well child awakens during the night with a cry and is seized with nausea, vomiting and pain, followed by mild diarrhea. These mild premonitory symptoms are usually not regarded seriously, but soon the fulminating course characteristic of adrenal hemorrhage appears, and this frequently proceeds rapidly to a fatal termination.

Cyanosis first appears. This may be constant or intermittent, and either generalized or limited to the lips and nails. Usually the appearance of this sign is accompanied by a rapid rise in temperature, but the temperature may not rise until later and may even be subnormal. Within a short time petechial mottling of any or all parts of the body appears. The petechiae are reddish and tend to increase and coalesce, especially about the hands and smaller joints of the body. Lesions of the mucous membrane and conjunctivas are often encountered. Frequently a post-mortem type of lividity is present in the dependent portions of the body. As the condition progresses the patient lapses into a state of profound shock, with a fast, irregular pulse, rapid respirations and a fall in blood pressure. A characteristic feature of shock of adrenal origin is that the extremities become cold whereas the body remains warm.¹ Commonly observed signs of the final phase consist of Cheyne-Stokes respiration, coma, delirium or convulsions, a sudden rise or fall in temperature and death, which may come on in twelve to

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sulfadiazine level of the spinal fluid was 11.6 mg. per 100 cc. No organisms could be cultured.

On admission the blood chloride was 514 mg. per 100 cc., the glucose 94 mg., and the nonprotein nitrogen 116 mg. A blood culture showed meningococci.

The urinary output during the first 24 hours was 15 cc. despite a 4000-cc. fluid intake. Catheterization produced only another 90 cc. That night the subcutaneous tissues were turgid and edematous and the output for the day was only 180 cc. Urinalysis that evening showed a heavy trace of albumin and large numbers of red cells. The nonprotein nitrogen was 103 mg. per 100 cc. Because of the possibility of large amounts of adrenocortical extract in conjunction with large amounts of saline causing fluid retention, these were stopped. Sulfadiazine anuria could not be ruled out, although this was not thought to be likely, but sulfonamide therapy was discontinued. Cystoscopy and ureteral catheterizations were negative. Following this the patient was given 105 cc. of polyvalent antimeningococcus serum. She became more edematous during the night and had periods of apnea and cyanosis. For this Coramine and caffeine were given intramuscularly.

On the 3rd hospital day the patient had marked and generalized edema. The urinary output had been 180 cc. during the night. She was unable to hear and had bilateral internal strabismus. The urinary output improved that day. The petechial spots, which had become greatly enlarged and coalescent, began to fade at the periphery. The systolic blood pressure had risen to 140, and the pulse was 90.

The course from this time on was one of gradual improvement without further serious complications. Six days following the administration of the antimeningococcus serum, polyarticular hydrarthrosis involving the knees and elbows appeared. Culture of the joint fluid was negative. The only other complications were the development of deep pressure sores over some of the petechial eruption under the heels and buttocks.

The patient had some residual joint stiffness, which improved with physiotherapy. At the time of discharge, 6 weeks after admission, she still had some stiffness in the knees, a slight hearing impairment and a mild degree of myopia. The spinal fluid was normal aside from an elevated protein value—75 mg. per 100 cc. There were still two deep pressure sores on the heels that had not filled in. She felt well.

On June 9, the patient reported for a check on her spinal fluid. The cell count, glucose and protein were normal. The hearing and vision had improved. The pressure sores were well filled in and there were no more joint symptoms. The patient had been at work for a week, and looked and felt well.

SUMMARY AND CONCLUSIONS

A case of purpura fulminans has been reported because of its rarity and especially because of the extremely low incidence of recovery.

It is evident that the syndrome is being oftener recognized clinically. Any patient, especially a young child, who develops spontaneously or in the course of a contagious disease cyanosis, purpuric eruption, profound shock and hyperpyrexia should be regarded as manifesting the syndrome.

Since the course of this disease is often rapid and fulminating, it is imperative that a prompt diagnosis followed by early and active treatment be carried out. In view of the high mortality, heroic measures seem justified.

Since the infection is usually bacterial in origin, the sulfonamides seem to be the mainstay of therapy.

Hormonal replacement with both adrenocortical extract and adrenalin are indicated in the hope of carrying the patient along until a hoped-for resumption of adrenal function takes place.

Plasma, blood transfusions and other supportive therapy may be indicated.

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INSTRUMENTAL REMOVAL OF A TWO AND A-HALF-POUND BLADDER CALCULUS, WITH RECOVERY*

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THE following case is reported because it records the largest bladder calculus ever removed with complete recovery. The dry weight of the calculus was 1134 gm (2½ pounds). It was composed of phosphates and carbonates.

The literature in regard to bladder calculi is copious, and only a few of the references¹ are appended. The search through it included the domestic and foreign literature and was conducted through the Yale Medical Library with microfilm material obtained from other sources notably the Army Medical Library and the New York Academy of Medicine.

The next largest stone reported is removed with survival is that of Smith,² which weighed 2 pounds, 6½ ounces. No follow up was given beyond the hospital stay. The 4 pound stone reported by Randall³ is the largest bladder calculus removed during life; the patient died thirty-six hours later.

CASE REPORT

The patient, a 34-year-old man, was admitted to the New Haven Hospital on October 28, 1940, with a chief complaint of pus in the urine. He had had urinary difficulty for the last 4 years characterized by hesitancy, slight dysuria, nocturia (one or two times), variation in the size of the stream, cloudy urine and occasional hematuria. He had recently lost 23 pounds in weight.

The past history was unimportant except that the patient had had weak kidneys as a child. He could recall no specific complaints. The family history was negative.

Physical examination on admission showed a man appearing slightly tired and rather old for his age. The temperature, pulse and respirations were normal. The blood pressure was 156/82. All the teeth were markedly carious. There was a stony, hard, rounded abdominal mass in the suprapubic region that extended almost to the umbilicus. On rectal examination the same mass was felt, as well as a small prostate just within the anus.

The urine was yellow and cloudy with a specific gravity of 1.015, a slight amount of albumin, no sugar and occasional red cells. It contained innumerable white cells with many cocci in clumps and many small rods in the methylene blue smear. In the only peroperative determination of the reaction of the urine it was reported as being acid to litmus paper, one of us (R. H. J.)

however knew that the urine was alkaline on at least one occasion.

An intravenous phenolsulfonphthalein test was done. No dye appeared in the urine 10 minutes after injection. 45 per cent appeared in 1 hour and 10 minutes and



FIGURE 1 Interoposterior View of the Cystolith

30 per cent in 2 hours and 10 minutes. The total percentage of dye in 2 hours and 10 minutes was thus 75 per cent.

The blood was normal. A Kahn test was negative. The nonprotein nitrogen was 31 mg per 100 cc., the blood calcium 10.5 mg and the blood phosphorus 3.4 mg.

Intravenous urograms showed bilateral hydronephrosis and hydroureters. There was a huge laminated, calcific shadow in the bladder region (Figs 1 and 2), but no calcifications in the kidney and ureteral regions.

Eight days after admission a suprapubic cystolithotomy was done under Avertin, nitrous oxide and oxygen anesthesia. A large, friable gray calculus was removed with the aid of obstetric forceps and a suprapubic tube was left in place. At the close of the procedure the blood pressure was 70/60 and the pulse 108. The patient responded well to a 500-cc blood transfusion and 5 per cent glucose given intravenously. Two grams of sulfathiazole was given daily for 2 weeks postoperatively, with blood levels between 0.5 and 2.3 mg per 100 cc. The oral temperature was never above 100.4°F.

The dry calculus was white and flaky, weighed 1134 gm and was composed of phosphates and carbonates.

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Cystoscopic examination 3 weeks after cystolithotomy showed a slightly constricted vesical neck, which was then resected with a Young's punch. The suprapubic tube was removed and a Foley indwelling catheter was left in place for 5 days. At discharge 10 weeks after

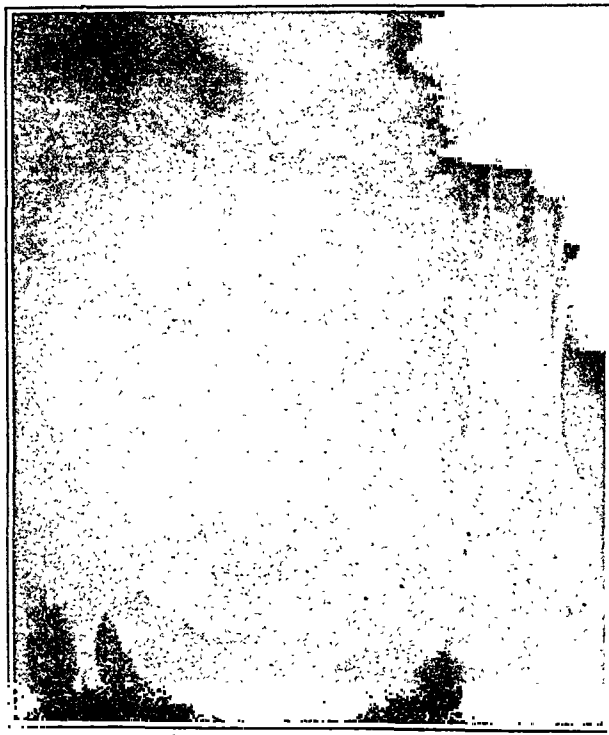


FIGURE 2. *Oblique View of the Calculus.*

operation, the suprapubic sinus was healed and the patient was symptom-free. There was 50-cc. residual urine, which contained many white cells and bacilli.

After discharge, the patient remained symptom-free and gained 30 pounds in weight. The urine was consistently infected with bacilli until a course of sulfadiazine cleared it in October, 1942, 2 years after removal of the calculus.

A complete cystoscopic examination with retrograde pyelograms later in the same month was entirely normal except for trabeculation of the bladder, which had been observed preoperatively. The urine was free from infection, and there was no residual urine. The blood pressure was 140/85. The urine was normal and without infection when the patient was last seen (December, 1942).

In view of the composition of the calculus (analyzed by the methods used by Higgins and Mendenhall¹), the reaction of the urine was somewhat of a puzzle. Three postoperative checks with nitrazene paper, while the patient was still in the hospital without medication and at various times of the day, showed the reaction to be pH 5.5. When the patient was last cystoscoped the reaction was pH 6.0, as tested with litmus, phenol red, brom-cresol green, brom-cresol purple and nitrazene paper. There is no explanation of this.

SUMMARY

A case report is presented of a thirty-four-year-old man from whom a 2½-pound bladder calculus composed of phosphates and carbonates was successfully removed. The hydronephrosis disappeared, the urinary-tract infection subsequently disappeared, and the patient became symptom-free.

This, to the best of our knowledge, is the largest bladder calculus removed with complete recovery that has been reported.

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Erratum. In the paper "Actinomycosis of the Chest with Spread to the Abdomen" by Drs. Ladd and Bill, which appeared in the November 11 issue of the *Journal*, the abbreviation "mg." should be changed to "gm." in three places: page 749, column 2, line 23, and page 750, column 1, lines 6 and 12.

MEDICAL PROGRESS

CURABLE FORMS OF HEART DISEASE*

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PATIENTS with the conditions discussed in this report comprise only a minority of all those with heart disease. The correct diagnosis, however, is most important, since therapy is highly effective in the majority of cases, whereas in the commoner varieties of heart disease treatment is generally far less satisfactory.

PATENT DUCTUS ARTERIOSUS

In 1939, Gross and Hubbard¹ reported the first successful ligation of patent ductus arteriosus in man; ample confirmation of the usefulness of the procedure is now available.²⁻¹¹ In addition, the renewed interest in this condition resulting from Gross's work has stimulated study of the disease.

Etiology. The ductus arteriosus (normally) is patent during intrauterine life; its persistence after birth is therefore not the result of a bizarre congenital malformation.¹² Kennedy¹³ recently demonstrated that closure involves two phases previously postulated by Wells.¹⁴ The first is due to a muscular contraction of the wall of the ductus, requiring several minutes; the second phase, obliteration by fibrous tissue, requires approximately one month. Breathing stimulates closure, and Kennedy¹⁵ has shown that the onset of normal breathing in animals is followed by closure in three to ten minutes. Oxygen bubbled into the umbilical vein of fetuses also results in closure of the ductus. He therefore concludes that high concentrations of oxygen in the arterial blood and the beginning of vigorous respiration just after birth presumably combine to promote prompt closure.

Incidence. Patency of the ductus is not rare. In the course of a few years Gross¹⁶ has operated on 56 patients with this condition. Keys and Shapiro^{8, 17} have studied 51 patients, and estimate that there are at least 20,000 persons with patent ductus arteriosus in the United States at the present time.

Clinical picture. Patent ductus arteriosus may be recognized clinically by the presence of a so-called "machinery" or constant murmur in the second left interspace, a systolic thrill in this area, dullness in the second or third left intercostal space and the peripheral signs of aortic insufficiency. X-ray study reveals a prominent conus shadow and, in almost all patients, some degree of dilatation of the left auricle, enlargement of the left ventricle, increased pulsations of the left ventricle and pulmonary artery, hilus dance and pulmonary congestion.^{4, 18} Electrocardiograms may show left-axis or right-axis deviation or none; when right-axis deviation is present, one must exclude the presence of some other congenital lesion.

Dynamics of the circulation. In man the diastolic blood pressure is usually low and the pulse pressure wide; mild exercise results in a further decrease of the diastolic pressure.¹⁹ No change in mean blood pressure occurs in animals with a long-standing fistula between the aorta and pulmonary artery.²⁰ The venous pressure in man shows no constant changes.¹⁹ The circulation time is somewhat longer than would be expected in the absence of congestive failure, and is explained on the basis of an increased amount of blood in the lungs.¹⁹ The vital capacity is unchanged. In animals an increase in total circulating blood volume is observed after the establishment of an aortic-pulmonary artery fistula.¹⁹ The cardiac output is increased as a result of a left-ventricular output two to four times higher than the right-ventricular output.¹⁹⁻²¹ Since the flow of blood under ordinary conditions is entirely from the aorta into the pulmonary artery, cyanosis is absent. During coughing, laughing, crying, straining at stool and so forth, however, changes in pulmonary intravascular pressure may cause the flow through the ductus to be reversed, resulting in transitory cyanosis.

Results of surgery on dynamics of circulation. At the moment of closure of a patent ductus, the diastolic blood pressure immediately increases,^{18, 22} probably owing to the diversion of the entire left-ventricular output into the aorta. The pulse rate slows, either because of increased vagal tone or, more likely, as a concomitant of the decrease in cardiac output.^{22, 23} There is a decrease and equal

*The articles in the medical progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III 678 pp., Spring Field, Illinois, Charles C. Thomas, 1942, \$5.00).

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ization of the cardiac output of both ventricles,¹⁹ lasting for at least twenty-seven minutes.²⁰ Blood samples taken from the pulmonary artery show a more marked degree of oxygen unsaturation than was present before closure.²⁰ The above-mentioned increases in circulation time and blood volume are restored toward normal following closure of the ductus.¹⁹

Clinical results of surgery. Reports by Burwell, Eppinger and Gross^{18, 19} indicate that enlargement of the heart due to dilatation, when present, disappears rapidly following surgery. Hypertrophic enlargement changes little in the immediate postoperative period. The cardiothoracic ratio, however, eventually becomes normal. Patients with definite congestive failure preoperatively show no symptoms of failure postoperatively despite a greatly increased physical activity.

The mortality of operation is low. Gross¹⁶ reported 2 surgical deaths in 56 operations. Complete division of the ductus, in addition to ligation, has been successfully accomplished in his last 14 cases. The advantage of division is the assurance of complete and permanent closure of the ductus.

Indications for surgical closure of patent ductus arteriosus. The majority of patients with patent ductus arteriosus die of cardiovascular complications; 25 per cent die with congestive failure, 25 to 33 per cent die with bacterial endarteritis, and 12 per cent die suddenly.²⁴

Burwell²⁵ has recently stated:

I think that any expression of opinion at this stage of our knowledge is bound to be tentative since we have been able to observe patients for only a few years after closure of the ductus arteriosus by operation. Two statements may be made:

First, the presence of important limitation or actual heart failure, the demonstration that the patent ductus is interfering with normal growth, or the presence of subacute bacterial endarteritis would seem to me to constitute firm indication for the operation.*

Second, because of the probable utility of the operation in preventing progressive overwork of the heart and in preventing bacterial endarteritis in a young person, I should consider the demonstration of uncomplicated patency to be in itself a strong suggestion that operation should be considered.

SUBACUTE BACTERIAL ENDARTERITIS SUPERIMPOSED ON PATENT DUCTUS ARTERIOSUS

Incidence. The occurrence of superimposed infection in patent ductus arteriosus is frequent. Reports^{8, 24, 26} indicate that from 20 to 40 per cent of all patients in whom the condition is recognized die with this complication.

*This statement is in agreement with the published reports of many observers.²⁶⁻²⁸

Diagnosis. The diagnosis is based on evidence pointing to the existence of patent ductus arteriosus: generalized evidence of toxemia, such as fever, tachycardia, leukocytosis, weakness and pallor³⁰; and the symptoms and signs of bacterial endocarditis—that is, splenomegaly and clubbing of the fingers. The course may be that of a protracted atypical pulmonary infection due to repeated small pulmonary emboli³¹ or may be characterized by manifestations of peripheral embolism, or both may occur. Peripheral blood cultures may be negative until the lungs are unable to filter out all the organisms, the pulmonary lesions break down and release organisms into the peripheral blood stream, and spread of the infection occurs to the greater circulation.

Therapy. Although it is not certain that surgical ligation or division of the ductus will prevent the subsequent development of bacterial endarteritis, this may well prove to be the case. To date there have been 3 cases of infection developing on a previously ligated ductus. One patient was reoperated on successfully³²; 2 died following the initial operation.^{4, 33} Graybiel et al.³⁴ reported the first attempt at surgical cure of subacute bacterial endarteritis complicating patent ductus arteriosus. At approximately the same time Keele³⁵ and Touroff³⁶ reported similar cases. Touroff has reported operations on 11 such patients thus far.^{27, 28, 37, 38} Of the 9 patients surviving the operation, 6 recovered from the infection. Burwell and Gross³⁰ have recorded the findings in 7 patients with patent ductus arteriosus and superimposed bacterial endarteritis. All were treated with chemotherapy—sulfapyridine, sulfathiazole or sulfadiazine—and with surgical closure of the ductus. One patient was cured on a medical regime before surgery was undertaken. The remaining 6 patients still had positive blood cultures when surgical closure of the ductus was performed. Two of these received no benefit from the combined medical and surgical therapy and subsequently died of their infection. The 4 remaining patients have apparently been completely cured, as evidenced by cessation of fever, repeatedly negative blood cultures, gain in weight and a resumption of normal activities. An additional case has been reported in which chemotherapy alone resulted in cure.⁴⁰ It is of interest that there have been several reports of cure of subacute *Streptococcus viridans* septicemia by excision of an arteriovenous fistula.^{41, 42}

It is evident that a higher percentage—approximately 67 per cent—of recoveries can be expected following chemotherapy and surgery together⁴³⁻⁴⁶ than has been reported from chemotherapy used alone or with heparin, or from any

other type of medical regime.^{47, 48} It may be concluded that when intensive treatment with the sulfonamides does not result in the disappearance of infection, both clinically and bacteriologically, within a short period of time—that is, approximately two weeks—surgical ligation of the ductus is indicated.

The contraindications to surgery are evidence that the patent ductus arteriosus compensates for another coexisting congenital cardiovascular anomaly, and evidence that the vegetations have already spread to the aortic or mitral valves. The presence of soft new murmurs or a positive peripheral blood culture (a few colonies) cannot, however, be accepted as absolute evidence of spread. It is clear that early recognition and prompt therapy will minimize its likelihood.

Mechanism of action of surgery. It has been shown that shortly after surgery blood cultures become sterile.^{27, 41} In some cases this has been true of the first blood culture taken ten minutes after ligation. It is possible that the lung acts normally as an efficient filter, since blood cultures from the pulmonary artery contain many more colonies than do those obtained from the aorta.⁴⁹ The efficiency of the lung as a filter may increase when the traumatizing effect of the higher aortic pressure on the lesion in the ductus or pulmonary artery is removed by ligation. It is also possible that the decrease in pulmonary-artery pressure, the slowing of the pulmonary-artery blood flow and the decrease in oxygen content of the pulmonary arterial blood are factors.

THE HEART IN NUTRITIONAL DEFICIENCY STATES

Although thiamine deficiency is a well-recognized cause of congestive heart failure,⁵⁰⁻⁵³ it is perhaps not so widely recognized that deficiency states may exist in patients with congestive heart failure due to intrinsic cardiac lesions. Anorexia, the dietary limitations, the anoxia and congestion of the gastrointestinal tract leading to impaired absorption and the possibly deficient storage and utilization of the substances comprising the vitamin B complex in the presence of impaired liver function combine to give rise to vitamin B deficiency in many cardiac patients with congestive failure. These patients exhibit a red tongue, cheilosis and absence or diminution of tendon reflexes and vibratory sense in the legs.

Pathologic physiology. Porter and Downs⁵⁴ recently pointed out that thiamine deficiency in man results in an increase in cardiac output, both absolute and in relation to the oxygen consumed, an increase in blood volume, a decrease in circulation time, an increase in oxygen consumption and elevation of the venous pressure. The decreased

arteriovenous oxygen difference and the decreased circulation time suggest the presence of an abnormally dilated peripheral vascular bed. The vital capacity is low and the blood pressure may be normal. Electrocardiographic changes are noted in almost all patients.⁵¹ These consist of tachycardia, a change in the direction of the T waves and a prolonged QT interval. These abnormalities tend to disappear after adequate administration of thiamine, suggesting the presence of a functional rather than an anatomic disturbance. It has, however, been shown that thiamine deficiency may be followed by focal myocardial necrosis^{55, 56} and cardiac hypertrophy.⁵⁷

Therapy. It has been pointed out by Hawes et al.⁵⁸ that effective therapy in oriental beriberi with cardiovascular dysfunction requires the use of large doses of vitamin B₁ parenterally. These authors stress the fact that in many cases enormous doses have been given by mouth with hardly any noticeable effect. Patients observed in this hospital support this contention. The following case is illustrative of the therapeutic effect of parenteral administration of thiamine chloride and vitamin B complex.

A. L., a 53-year-old man, entered the Beth Israel Hospital on June 27, 1943, with a history consistent with rheumatic fever at the age of 12. Twenty-seven years before entry he had been refused life insurance because of some cardiac abnormality. Ten years before entry he began to experience increasing fatigability, mild dyspnea on exertion and occasional edema of the ankles. About 1 year before admission these symptoms increased and during the previous 6 months dyspnea, both exertional and paroxysmal, orthopnea and peripheral edema became severe and progressive. Marked anorexia and a weight loss of 25 pounds were evident during the previous year. Treatment prior to hospitalization consisted of digitalization, intermittent bed rest and injections of Mercupurin. His condition, however, became so severe that he entered the hospital.

The essential findings were as follows: temperature, 99°F.; pulse, 70; respirations, 25; and blood pressure, 160/60. The patient was pale and cachectic, perspiring profusely, and exhibited severe dyspnea and orthopnea. Slight icterus, moderate cyanosis and marked venous engorgement with prominent venous pulsations were evident. There were redness and atrophy of the tongue as well as cheilosis. The anteroposterior thoracic diameter was increased, and diminished resonance, voice sounds and breath sounds, as well as fine crackling rales, were noted over both lung bases. The heart was tremendously enlarged to both left and right, with a widespread bounding apex impulse in the left axilla. The head bobbed and the chest wall heaved with each heartbeat. Characteristic murmurs of aortic and mitral stenosis and insufficiency were heard. The second aortic tone was almost inaudible. The liver was enlarged a handbreadth below the right costal margin and was firm and moderately tender. Slight clubbing of the fingers, bounding radial pulses and marked pitting edema of the legs, with a small amount of sacral edema, were apparent. The knee

jerk reflexes were sluggish. The Achilles tendon reflexes were not obtained.

Examination of the urine revealed normal findings, except for a slight trace to a trace of albumin during the first days. The blood counts were normal. The blood nonprotein nitrogen was 53 mg. per 100 cc. on admission, rising to 82 mg. during the next 3 days and subsequently returning to normal. The circulation time (calcium gluconate) was 60 seconds. The total blood protein was 6.9 gm. per 100 cc. A 7-foot roentgenogram showed the transverse diameter of the heart to be 21 cm. (twice the expected diameter for the patient's height and weight). The pulmonary arteries were prominent, the left auricle moderately dilated, and the pulmonary vessels dilated. Electrocardiograms showed left-axis deviation, a prolonged PR interval (0.22 seconds), depressed ST₁ and ST₂, inverted T₁ and T₂, and auricular and ventricular premature beats.

On admission oxygen was administered by mask, re-digitalization was accomplished, and ammonium chloride and vitamin B complex (6 capsules a day) were given. Dyspnea, marked heat intolerance and apprehension increased. Mercupurin, given intravenously on the 4th day, resulted in a diuresis of 4500 cc. in 24 hours. In spite of this, the course during the next 9 days was downhill. Increasing edema, severe dyspnea at rest, growing intolerance of the summer heat and several psychotic episodes were noted. There was no diuretic response or change in the clinical picture following the subsequent intravenous injection of Mercupurin. On the 13th day all oral vitamin B was omitted, and 100 mg. a day of intramuscular thiamine hydrochloride and 1 cc. of vitamin B complex were begun. Within 36 hours a striking change in the clinical picture took place. The dyspnea became minimal, the very severe heat intolerance disappeared although the weather was warmer, and the patient had no more psychotic episodes. During the course of the next 6 days the pulmonary rales disappeared and the peripheral edema became clinically undetectable following a favorable response to Mercupurin injection. The oxygen tent was omitted 2 days after institution of parenteral vitamin therapy. In addition the patient developed an appetite for food. The parenteral vitamin therapy was omitted after 8 days and vitamin B complex (6 capsules) and 15 mg. of thiamine hydrochloride were given orally. Mild to moderate dyspnea and slight to moderate pitting edema began to appear about 10 days after the omission of the parenteral vitamins. The patient was discharged on the 38th day much improved, but with slight dyspnea at rest and slight pitting edema of the ankles and sacrum.

Equally favorable effects on dyspnea and psychosis have been noted following administration of thiamine hydrochloride and vitamin B complex parenterally in other patients with vitamin B deficiency and severe organic heart disease causing long-standing decompensation with severe dyspnea after failure of the usual treatment with digitalis, diuretics and oxygen to secure improvement.^{59, 60} No striking benefit has been noted after the administration of large amounts of vitamin B complex, including thiamine, by mouth for periods from a few weeks to several months or more.⁵⁹

CHRONIC CONSTRICTIVE PERICARDITIS

Chronic constrictive pericarditis is recognized by the presence of a small or only slightly enlarged heart, diminished heart tones, markedly increased venous pressure and an enlarged liver with ascites. Blalock and Burwell⁶¹ and Harrison and White⁶² have recently reported follow-up studies on their series of cases of constrictive pericarditis, and conclude that approximately 60 per cent of all cases may be cured by surgical excision of portions of the scar. Although the surgical mortality rate is low,^{61, 63} it is of further interest that both groups of investigators stress the point that not all patients need surgery; if the disease is not progressive and the disability is mild, patients do well on salt restriction, diuretics and tapping of serous cavities. Digitalis is of no value except when myocardial weakness or auricular fibrillation is present.⁶¹

Pathologic physiology. Thickening and contraction of the pericardium or epicardium or both prevent the heart from dilating normally and therefore decrease the amount of blood received during diastole. There may also be some interference with emptying of the heart. It has recently been demonstrated that chronic compression of the heart results in atrophy of disuse, manifested by smaller muscle fibers.⁶⁴ The decreased filling, with increased venous pressure, results in an increase in pulse rate (Bainbridge reflex). The decreased output and inability to increase it normally result in weakness, fatigue, tachycardia, low pulse pressure and a diminished tolerance for exercise. The increase in venous pressure leads to the peripheral signs of venous congestion. The circulation time is prolonged and the arteriovenous oxygen difference⁶⁵ is increased. Hitzig⁶⁶ has recently offered an explanation of the occurrence of pulsus paradoxus in constrictive pericarditis: If the compression is predominantly right-sided, the phenomenon of pulsus paradoxus appears when there is a marked discrepancy between the pulmonary blood volume during expiration and the pulmonary vascular capacity during inspiration. This results in inadequate left ventricular filling and a decreased output with a weakened beat.

The electrocardiograms in White's⁶² series showed normal rhythm in 60 per cent and auricular fibrillation in 37 per cent of patients. Low voltage of the QRS complex was found in 60 per cent, with little change following surgery. Abnormal T waves in two or three of the classic leads were found in all cases; none of the T waves became normal in more than one lead following surgery. The electrocardiogram during pericardiectomy

has been studied by Stewart and Bailey.⁶⁷ Premature beats and paroxysms of abnormal rhythm, such as auricular fibrillation, auricular flutter and tachycardia, as well as ventricular tachycardia, were observed. The changes were of short duration and were similar to those previously recorded by Feil and Rossman.⁶⁸ Serial electrocardiograms taken for months after operation showed few changes in the form of the T waves or ST segments.⁶⁷

WOUNDS OF THE HEART AND VESSELS

Trauma to the heart. The war has resulted in increased interest in cardiac trauma.⁶⁹⁻⁷³ In such cases the early recognition of cardiac tamponade is most important. A large, quiet heart, an increase in venous pressure, or rapid pulse rate, a drop in blood pressure with a low pulse pressure, cyanosis and orthopnea are evidences of cardiac compression.

The Army⁷⁴ has recently formulated the treatment of penetrating heart wounds as follows: Blood must be aspirated from the pericardium by the costoxiphoid route, if possible within two hours of the onset of the tamponade. The advantages of the costoxiphoid route are that the needle avoids passing through both pleural leaves, that one cannot injure the lingula of the upper lobe if it is adherent, and that the pericardial sac can be more satisfactorily cleared of blood.⁷⁵ After anesthetizing—with 1 per cent novocain—the skin and underlying tissues, a 15-gauge, short-beveled needle is inserted at the left costoxiphoid junction and directed inward and slightly upward until blood escapes. Either a small syringe or no syringe should be attached to the needle. If the needle touches the heart, a scratching sensation is felt, and the needle must immediately be slightly withdrawn. Paracentesis may be done at the site of injury, if indicated, since even the withdrawal of a small amount of blood may be lifesaving. Several reports are available noting the beneficial effects of conservative treatment by means of aspiration and plasma, blood and saline infusions.⁷⁶⁻⁷⁸ Recurrence of tamponade is an indication for a second paracentesis. This should not be done less than fifteen minutes after the first in order that closure of the wound by a clot may be favored. If tamponade again recurs, extra-pleural cardiorrhaphy is indicated. The mortality rate from this operation in experienced hands varies from 26 to 50 per cent.^{71, 76}

It is now accepted that contusion of the heart may be consequent on nonpenetrating trauma to the chest wall. An interesting variant is afforded by a case of intrauterine cardiac injury produced by a nonpenetrating blow to the maternal abdomen, with the death of the fetus.⁷⁹ In addition,

Scherf and Terranova⁸⁰ have recently shown that displacement of the ST segment of the electrocardiogram occurs following blunt trauma to the precordium. The traumatic nonpenetrating wounds of the heart may present the following clinical features: absence of symptoms, with complete recovery; delayed, fatal rupture of the heart; myocardial failure, both transient and persistent; hemopericardium; ruptured valve; coronary thrombosis and acute myocardial infarction; angina pectoris, both transient and persistent; and arrhythmias, both transient and persistent, particularly auricular fibrillation.⁸¹⁻⁸⁴ The recognition of the possibility of cardiac damage after blunt trauma to the chest should be emphasized. The absence of bruising or other external evidence on the chest wall should not be construed as excluding cardiac trauma. Adequate treatment in the form of bed rest, oxygen administration, sedation and paracentesis may result in complete clinical recovery.

Traumatic arteriovenous aneurysms. The effects of an arteriovenous fistula on the circulation are similar to those noted above for patent ductus arteriosus. In arteriovenous fistula, however, since the systemic circulation is involved, the ventricular outputs are equal, and an increased blood flow is present in both the systemic and pulmonary circuits. Many case reports of successful repair of such fistulas have been published.⁸⁵⁻⁸⁷ Occasionally, however, spontaneous healing occurs.^{88, 89} It is important to remember in this connection that congestive heart failure may occur months or years after the establishment of an arteriovenous fistula.⁸⁷ Surgical removal of the fistula results in disappearance of the signs and symptoms of congestive failure.^{88, 87, 89} Reid and McGuire⁸⁸ emphasize the importance of prolonged bed rest with elevation of the affected part and postponement of surgery for three to six months. During this time hemorrhage becomes absorbed, the tissues are restored toward normal, the danger of infection is lessened, and collateral circulation develops.

There have been to date two reports of cures of subacute *Streptococcus viridans* septicemia due to an arteriovenous endarteritis by excision of the fistula.^{41, 42}

CARDIOVASCULAR SYPHILIS

Cardiovascular syphilis can be prevented in 99 per cent of patients by the prompt and energetic treatment of early syphilis.^{90, 91} It is important to recognize that adequate treatment of cardiovascular syphilis is effective only before serious complications arise. The criteria for the diagnosis of uncomplicated syphilitic aortitis are teleroentgenographic and fluoroscopic evidence of aortic dila-

jerk reflexes were sluggish. The Achilles tendon reflexes were not obtained.

Examination of the urine revealed normal findings, except for a slight trace to a trace of albumin during the first days. The blood counts were normal. The blood nonprotein nitrogen was 53 mg. per 100 cc. on admission, rising to 82 mg. during the next 3 days and subsequently returning to normal. The circulation time (calcium gluconate) was 60 seconds. The total blood protein was 6.9 gm. per 100 cc. A 7-foot roentgenogram showed the transverse diameter of the heart to be 21 cm. (twice the expected diameter for the patient's height and weight). The pulmonary arteries were prominent, the left auricle moderately dilated, and the pulmonary vessels dilated. Electrocardiograms showed left-axis deviation, a prolonged PR interval (0.22 seconds), depressed ST₁ and ST₂, inverted T₁ and T₂, and auricular and ventricular premature beats.

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not revert may then be treated with quinidine. On the other hand, the Massachusetts General Hospital group¹⁰⁸ gives quinidine preoperatively, except to those patients with active auricular fibrillation, beginning twenty-four hours before surgery and continuing for twenty-four to thirty-six hours thereafter. They also stress the importance of reassuring the patient regarding the entire operative procedure, the anesthetic, the postoperative discomfort, intravenous injections and the oxygen tent.

ANEMIA AS A CAUSE OF CARDIAC PAIN AND CONGESTIVE FAILURE

An erroneous diagnosis of heart disease is often made in patients with anemia¹⁰⁹ because of dyspnea, easy fatigability, weakness, precordial pain,¹¹⁰ murmurs that simulate those of mitral stenosis¹¹¹ and edema. It is true, however, that severe anemia of any origin may have a harmful effect on a normal or diseased heart because of the persistent marked increase in cardiac work consequent on a decrease in the hemoglobin level below 50 per cent.¹¹²⁻¹¹⁴ It is sometimes difficult to differentiate dyspnea due solely to an inadequate amount of circulating hemoglobin from that consequent on congestive heart failure in a severely anemic patient. The presence of rales, orthopnea and venous engorgement in the latter condition and their absence in the former¹¹⁵ are very helpful.

Incidence. A recent study by Riseman¹¹⁶ has shown that anemia, thyrotoxicosis and polycythemia occurred in his clinic in a total of less than 1 per cent of patients with angina pectoris. There are, however, many patients with anemia whose presenting complaints are those of angina pectoris or congestive failure. Thus, from 1918 to 1937, Stalker¹¹⁷ collected 100 cases of angina pectoris and pernicious anemia. Since 1937, several reports indicate the not uncommon association of angina pectoris and hypochromic anemia.^{118, 119} Congestive failure precipitated by anemia appears to be less common, since only a small number of cases have been recorded.^{111, 115, 119}

Pathologic physiology of the circulation. The effects of anemia on the circulation resemble in some ways those produced by thyrotoxicosis or an arteriovenous shunt. The systolic and diastolic blood pressures are lowered,¹⁰⁹ with an increase in pulse pressure probably due to peripheral vasodilatation and a decreased blood viscosity. The circulation time is more rapid,^{120, 121} although it may be normal in the presence of congestive failure,¹²² and the cardiac output and oxygen utilization are increased.^{112, 114} Considerable cardiac enlargement occurs in approximately 50 per cent of

patients and is particularly common in the older age group.¹⁰⁹ Although most of the enlargement is due to dilatation, some hypertrophy apparently occurs.¹²³ The electrocardiograms may show flattened or inverted T waves, depression of the ST segments, particularly in Leads 1 and 2,^{109, 124} tachycardia, auricular ventricular nodal rhythm¹⁰⁸ and prolongation of the QT interval.¹¹⁵ These phenomena are responsible for the tachycardia, dyspnea, increased fatigability, weakness and edema noted in anemic patients. A contributory factor in the genesis of edema may be the decreased blood total protein with a reversal of the albumin-globulin ratio seen in some patients.¹¹⁵ Although most anemic patients with angina pectoris have underlying organic heart disease, several reports stress the normality of the coronary arteries in such patients.^{125, 126} The anemia, with its consequent reduction in oxygen capacity, results in myocardial anoxemia and chest pain.

Response to therapy. It is universally agreed that blood transfusions,¹¹⁸ iron, liver and bed rest result in cure in almost all cases, whether the symptoms are those of congestive failure or of angina pectoris. The changes in the circulation, size of the heart and electrocardiograms noted above are restored to normal. This of course indicates that the changes induced by anemia are functional rather than organic in nature. Although bed rest may not be necessary for all patients,¹²⁷ in some cases of congestive failure its use together with digitalis and diuretics may be required to tide the patient over until the hemoglobin level increases significantly in response to antianemic therapy.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

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CASE 29501

PRESENTATION OF CASE

A sixty-year-old housewife entered the hospital because of rectal bleeding.

The history was taken through an interpreter and was rather incomplete. The patient had been in good health until about one year prior to admission, when she had an episode of "moderate" rectal bleeding. There was no pain or "any other symptoms." It is not stated how long the bleeding lasted. Since that time she had had two similar episodes. At various other times she had noticed that her stools were blood streaked. Her bowels had always been regular. She had had no diarrhea and rarely took cathartics. Her appetite had been good. There was no vomiting, but occasional regurgitation of food after eating. There had been no weight loss. In the few months preceding entry she had a more or less constant ache in the right side of the abdomen, "just opposite the umbilicus," which was usually accompanied by gaseous distress. Two barium enemas performed at an outside hospital were said to have shown a polypoid filling defect in the lateral wall of the ascending colon just above the ileocecal valve.

She had had a hysterectomy eighteen years before entry, and a right nephrectomy sixteen years prior to admission following an attack of severe right flank pain. No diagnoses were recorded for either operation, and no additional information was available.

Physical examination showed a well-developed, rather obese woman in no distress. The lungs were clear. There was a Grade 2 aortic systolic murmur. The aortic second sound was greater than the pulmonic. The abdomen was not distended. Peristalsis was normal. No masses could be palpated. There was tenderness with some spasm deep in the right side of the abdomen at the level of the umbilicus. The scars of the previous operations were well healed. There were no hernias.

*On leave of absence.

The blood pressure was 140 systolic, 82 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood showed a white-cell count of 10,600, with 56 per cent neutrophils and 39 per cent lymphocytes. The hemoglobin was 13 gm. A blood Hinton test was negative. The urine was negative. The stools were guaiac negative. The blood sugar was 68 mg. per 100 cc., the nonprotein nitrogen 10 mg., and the total protein 7 gm.

An abdominal exploration was performed on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD H. SWEET: I wonder if it was accurate to describe the filling defect as being polypoid. In examining an x-ray film Dr. Holmes has taught us to describe what we see and then go to the diagnosis. I assume there was more than one x-ray observation.

The record does not say whether this patient was admitted under the care of a medical service or under the care of the surgeons. I should not mention that except that a great deal of reliance must be placed in some of these histories on the interpretation of physical findings, and my medical friends are not always certain of their own evaluation of such things as tenderness and spasm in abdominal lesions. They sometimes call the surgeon in. The record does not say, furthermore, whether any x-ray films were taken in this hospital.

DR. BENJAMIN CASTLEMAN: We have the films from the other hospital. Perhaps Dr. Mueller will comment on them now.

DR. H. PETER MUELLER: I examined this patient in an outside hospital and found this lesion, which has the appearance of a polypoid mass (Fig 1). In addition to this round, filling defect, which appears to be opposite the ileocecal valve, the patient was definitely tender on palpation. I was not quite sure when I saw the films for the first time whether this meant anything, or whether it was just due to an enlarged ileocecal valve. I repeated the x-ray films a few days later and the same findings were observed. I had the impression that the filling defect seen in the spot films was too large for the ileocecal valve and that it was probably due to a polypoid mass.

DR. SWEET: What do you mean by "polypoid"? Do you refer to the configuration of the shadow, or to the fact that the lesion appears to hang from the wall of the bowel?

DR. MUELLER: I had the impression that a mass

with a broad base was projecting from the wall of the bowel into the lumen

DR SWEET Above the level of the cecum in the ascending colon?

DR MUELLER Yes

DR SWEET The record states that a mass was felt. The patient was an obese woman, hence it

health. Therefore, without much help from the history and little help from the physical examination, I must guess what this might have been.

If it were a mass, and from the x-ray findings, I assume it was, we are fortunate to have the roentgenologist here who did the examination. It is interesting that he was uncertain at first and re-

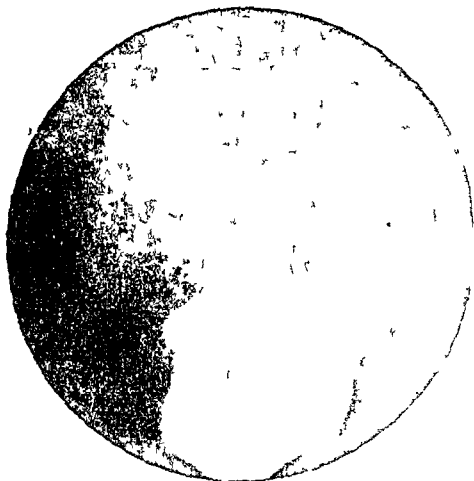


FIGURE 1 Spot Film Showing Filling Defect in Region of Ileocecal Valve

must have been quite a mass if they were able to feel it.

There is not much information in the record, and I can summarize it quickly. The patient had rectal bleeding, but there were periods when she had none. In this hospital the stools showed no blood on chemical examination. That is unlike a carcinoma. I should expect rather constant, at least microscopic or chemical, evidence of blood in the stools in a case of carcinoma of the colon. Furthermore, the history is not at all suggestive of carcinoma of the colon, except that the patient had had some bleeding. She could not have bled much because there was relatively no anemia.

On physical examination it is stated that the mass was tender. I am not accustomed to thinking of masses within the abdomen as being tender unless there is an inflammatory process, such as gangrene, inflammation from an ulcerated tumor or something of that sort. The normal blood chemistry, the general state of well being, the state of nutrition and the lack of weight loss seem to indicate that this woman was in remarkably good

health. To me it looks like a mass producing a filling defect in the ascending colon. Although I was prepared to appear before you and say that I could see no way of making a diagnosis in this case, after seeing the x-ray films, I am willing to say that the patient probably had a benign tumor of the ascending colon. The location is too high for a lesion around the appendix, a diagnosis that we occasionally make with a tender mass in the region of the cecum. Furthermore, to me it does not look like a tuberculous lesion. Those are the conditions that sometimes confuse us in the region of the right colon. I should say that this patient had a benign tumor in the ascending colon, the exact nature of which I do not know.

CLINICAL DIAGNOSIS

Polyp of ascending colon

DR. SWEET'S DIAGNOSIS

Benign tumor of ascending colon

ANATOMICAL DIAGNOSES

Submucous lipoma of ileocecal valve.
(Chronic intussusception.)

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: I am going to ask Dr. Allen to discuss his case and then take up the pathology of both cases together.

CASE 29502

PRESENTATION OF CASE

A forty-seven-year-old housewife was admitted to the hospital because of abdominal distress and vomiting of many years' duration.

During her childhood the patient was underweight and had occasional vomiting. At eighteen years of age she began to have attacks of distention, eructation, generalized abdominal pain, nausea and vomiting. The pain was most noticeable in the epigastric region and radiated through to the back and up and down the spine. The vomitus was never blood stained, nor did it contain coffee-grounds material. Vomiting occurred usually in the early evening but occasionally within five minutes of eating, especially after the ingestion of foods containing eggs and bananas. It was extreme and continued until dry retching occurred. The morning afterward she felt weak and dizzy, but there was no residual nausea. The bowel habits were regular but she was unable to describe their character. There was no change in the color of the urine. She had never been jaundiced. The attacks were not relieved by hot water or soda. She sometimes "lost as much as 12 pounds during a single attack." She had never been seen by a physician during an attack. About one month before entry she noticed severe right-sided abdominal pain, which was more prominent in the lower quadrant than in the upper and which apparently came on in the evening. "The pain felt like something would burst"; it was continuous for twenty-four hours and was associated with considerable vomiting. No medical advice was sought. It was not known whether she had had any more attacks. She remained in bed for the eighteen days before admission.

The patient was known to have had high blood pressure for many years. She had had occasional episodes of severe coughing productive of considerable sputum, which was occasionally blood tinged. Her mother was said to have had frequent "bilious attacks" with the vomiting of yellowish-green material. One sister had suffered from "stomach trouble."

Physical examination showed a slightly obese, well-developed woman in no distress. The heart

was slightly enlarged, with the sounds regular and of good quality; a systolic murmur was heard in the right third interspace. The lungs were clear. The liver edge was palpable three fingerbreadths below the costal margin and was quite tender.



FIGURE 1. Spot Film Showing Mass in Region of Ileocecal Valve.

Another point of tenderness was elicited by one examiner in the right lower quadrant. There were no masses, spasm or rebound tenderness in the abdomen. Examination was otherwise not remarkable.

The blood pressure was 210 systolic, 96 diastolic. The temperature was 97.4°F., the pulse 88, and the respirations 22.

Examination of the blood showed a red-cell count of 4,500,000, with a hemoglobin of 15.6 gm. The white-cell count was 8500, with 65 per cent neutrophils. The urine was negative. A phenol-sulfonephthalein test was normal. The stools were tan colored and guaiac negative. The blood nonprotein nitrogen was 19 mg. per 100 cc. A blood Hinton test was negative. A Graham test showed a 1.5-cm. area of calcification in the gall bladder, which had the appearance of a stone. The gall bladder failed to concentrate the dye.

A barium enema showed ready passage of the barium to the cecum. Arising from the lateral wall of the cecum, opposite the ileocecal valve, was a sharply defined, round mass, measuring 2 cm. in diameter (Fig. 1). The mass was constant and was well visualized after air injection. A gastrointestinal series and an intravenous pyelogram were negative.

On the fifth hospital day an abdominal exploration was performed.

DIFFERENTIAL DIAGNOSIS

DR. ARTHUR W. ALLEN: May we have the x-ray demonstration at this time?

DR. GEORGE W. HOLMES: The striking thing about this case, it seems to me, is a comparison of the films taken in the usual way, after the ingestion of barium with the colon filled, and the films taken after evacuation with air in the colon. When we carry the examination a little farther and use the pressure technic and spot film we begin to see something obviously wrong in this area here. This film was taken with the cecum distended with air; this film was taken with the cecum distended with barium; and this film (Fig. 1) shows the cecum partially empty. In the text it states that the lesion was opposite the ileocecal valve. The man who did the examination had a better opportunity to determine the position than I have, but I think that the important lesion is in the region of the ileocecal valve, not opposite it. If this is correct the shadow may be due to protrusion of the ileum into the cecum. If it is opposite the valve, it must be a mass arising from the wall of the cecum. One can get all the appearances of a filling defect from a slightly edematous ileocecal valve. In the July number of the *American Journal of Roentgenology*, Golden* illustrates cases that look not unlike this that were found to be due to edema of the ileocecal valve. There is no question about this lesion in the spot films. I do not believe this is a polyp protruding from the wall.

DR. ALLEN: The patient gives such a perfect story for cholelithiasis with acute inflammation and perforation into the hollow viscus, with the possibility of gallstone ileus, that I strongly suspect that there was something else the matter with her. Every time we see gallstone ileus in the ward we always say afterward that, had we been alert concerning the history of the case, we could have made the diagnosis without any question of doubt.

This woman of forty-seven had had a sensitive gastrointestinal tract since childhood. Her mother had had frequent bilious attacks, and her sister,

stomach trouble. Recently I was asked to operate on the wife of a physician for gallstones. I was told that no x-ray examination had been made and the husband of the patient said: "It is not necessary. You have already operated on her mother and two of her sisters for gallstones. Besides, she has a good clinical story." This woman's early attacks were very mild and not associated with cholecystic disease. Many children vomit periodically while they are growing up, and I thought that this mass might conceivably show calcified mesenteric nodes on the x-ray films. It would have been a good sequence for her childhood disorders. At the age of eighteen, however, she began to have attacks that sound more like gallstone colic, brought on by the ingestion of foods containing a high content of fat. It is interesting that at no time during her previous life when she had these episodes or at the time of her present illness, which started a month prior to admission, had she consulted a physician. Most people who have gallstone attacks do consult a physician, usually in the middle of the night during their acute distress. Perhaps the scarcity of doctors might have played a role in her not having a physician on the night that the last acute attack started. She was apparently quite ill at that time. She was conscious of a feeling of something being radically wrong. She felt as though "something was going to burst" which, incidentally, is an interesting statement and is perhaps leading me off "on a limb." She obviously was ill because she stayed in bed eighteen days after this episode, which is about the right time for a patient with gallstone ileus to appear in a hospital, usually with vomiting and usually with a gallstone stuck about 40 cm. from the ileocecal valve, in the portion of the ileum that is narrower than the rest of the small intestine. During its descent the gallstone collects a certain amount of fecal matter on the outside, and by the time it gets to this narrow segment it may produce obstruction of the small bowel. That is the story that these patients are most apt to give. We have no history here to indicate that at any time this affair caused small-bowel obstruction. According to the story the patient certainly did not have small-bowel obstruction when she entered the hospital, nor was she extremely ill. It is a little amazing that she had a normal temperature and pulse and did not have much in the way of physical signs, except for possible tenderness in two areas—one in the region of the right upper quadrant and one in the region of the right lower quadrant. So she could, I think, have had a gallstone that had left the gall bladder, had entered the gastrointestinal tract and was discovered

*Golden, R. Enlargement of ileocecal valve. *Am. J. Roentgenol.* 50:19, 1943.

in the region of the cecum at the time of admission.

There are a great many other things that might explain the local picture in this region. This woman had had no history of bleeding from the bowel. She was free from anemia—as a matter of fact she had 15.6 gm. of hemoglobin at entry, which is above normal. That brings up the question of tumors of the right bowel, which are supposed to cause anemia but which, as a matter of fact, only cause anemia in about 70 per cent of the cases. This could perfectly well have been a benign tumor, such as a lipoma, a lipofibroma or a true fibromyoma, or a benign polypoid lesion, although I strongly suspect that it was not of that type because she came to the hospital following an acute episode. This type of tumor does not cause an acute episode, except for intussusception, which does not permit a patient to stay in bed eighteen days prior to admission to the hospital; but an inflammatory lesion such as appendicitis could. That also could produce a defect similar to the one that we see here, but if the defect were still present from such cause I should expect that there would still be some leukocytic elevation, some elevation of temperature and some obvious tenderness in this region. Besides, in this film one sees a perfectly normal appendix. So I shall rule out appendicitis. Occasionally a single diverticulum of the intestine with diverticulitis occurs in this site. These cases produce symptoms and signs of acute appendicitis and are always diagnosed acute appendicitis preoperatively. The history is usually shorter than this and associated with a perfectly typical febrile reaction and a tender inflammatory mass. Therefore, I shall rule that out.

I am going to go back to the gallstones in this case: the history is so perfect for gallstone ileus, and about the right time had elapsed after the severe onset. One gallstone was left behind, and although the mass in the cecum does not look like a gallstone to me, I am going to assume that there was a gallstone in the cecum at the time of operation.

DR. HOLMES: The patient had a barium meal, and it went through without difficulty.

DR. ALLEN: I should expect a barium meal to show the biliary system if she had a fistula. Did you purposely keep back the gall-bladder films?

DR. HOLMES: No. I did not put them up because they do not show anything. If the patient had gallstone ileus, she should have shown some obstruction.

DR. ALLEN: Yes; I should assume there was no small bowel obstruction from the appearance of the flat film. No loops of small bowel are apparent.

DR. HOLMES: I should have put up the other film. I neglected to do so because it did not show anything. But you notice the barium passed through the ileum all right and entered the cecum.

DR. ALLEN: That would be expected if the gallstone had gone by, but I should like to see a little barium in the biliary tree.

CLINICAL DIAGNOSES

Cecal polyp.

Chronic cholecystitis and cholelithiasis.

DR. ALLEN'S DIAGNOSES

Gallstone in cecum.

Cholelithiasis.

ANATOMICAL DIAGNOSES

Hypertrophied ileocecal valve.

(Chronic intussusception.)

Cholelithiasis.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: In the case that Dr. Allen discussed the patient was operated on and the surgeon found the gall bladder filled with stones. There was no connection that he could make out between the gall bladder and the duodenum or the jejunum. When he felt the cecum he was able to palpate a definite mass. On opening the cecum he found a prolapse or protrusion of the mucosa (and possibly of the entire wall) of the terminal ileum into the cecum for a distance of 2.5 to 3.5 cm. The edge of the protruding tissue was everted. The whole mass of tissue resembled the end of a cornet horn. The examining finger passed freely through the lumen of the protruding tissue into the terminal ileum. No obstruction was felt. It was thought that any procedure toward removal of the lesion would necessitate an ileotransverse colostomy and right colectomy in a two-stage operation. Since the patient had hypertensive heart disease and since there was no obstruction in the ileocecal region no further surgery was deemed advisable at that time.

The patient left the hospital and was apparently free from symptoms for over two years, when she died of a cerebral hemorrhage.

In the case discussed by Dr. Sweet, the surgeon did not open the cecum. He felt the mass and resected the cecum and the terminal ileum. When the specimen was opened, the mass was found to be an ovoid, well-circumscribed, submucosal tumor involving about a third of the circumference of the ileocecal valve and projecting about 0.7 cm. above the rest of the valve. The mucosa over the lesion was definitely hemorrhagic. When sectioned the mass proved to be a lipoma. In

the serosa over both ileum and cecum there were many areas of fat necrosis. This, together with the mucosal inflammation, is evidence that something had been going on, and certainly the likeliest process is chronic intussusception.

The problem in Dr. Sweet's case is to decide whether the mass was a true lipoma or merely a hypertrophied ileocecal valve, with perhaps more than the usual amount of submucosal fat, similar to the one found in Dr. Allen's case. In going through some of our routine autopsies we have found hypertrophied ileocecal valves that had been removed from patients who had had no symptoms of chronic intussusception. These ileocecal valves are fatty and uniformly enlarged, unlike that in Dr. Sweet's case, in which the lesion was circumscribed and had produced a localized elevation of the mucosa. The case discussed by Dr. Sweet I think should be called a true lipoma, although I admit that I am not sure it could not have been merely a variation from the normal ileocecal valve. We have seen several other obvious submucosal lipomas in the intestinal tract, especially in the cecum and ascending colon. These were much larger than the one under discussion today and had produced intussusception. I believe that in the case discussed by Dr. Allen the patient had a hypertrophied ileocecal valve that also produced chronic intussusception.

Dr. ALLEN: I should like to ask Dr. Holmes if he considers the case I discussed as typical of

the cases Golden described. I think he spoke of mucosal edema and not of fat deposits.

Dr. HOLMES: That is correct.

Dr. ALLEN: It seems to me that these cases represent either an unusually large ileocecal valve or a small herniation of the terminal ileum through the valve. Is it not true that we may see a considerable variation? We have no good idea of what they are normally. How do you reconstruct the acute episode starting one month prior to entry?

Dr. CASTLEMAN: The patient probably was not sick because of her ileocecal intussusception. She was a severe cardiac and undoubtedly went to bed for any mild complaint. I believe that she had intussusception off and on, which reduced itself spontaneously. She remained free from symptoms for almost two years after operation.

Dr. HOLMES: The radiologist is more or less responsible for getting the surgeons into difficulties, and we must eventually be able to recognize this condition and to distinguish it from true tumor of the cecum.

Dr. CASTLEMAN: Does it matter whether you call it a true tumor or a variation from the normal? If it produces chronic intussusception, perhaps something should be done surgically.

Dr. HOLMES: The points are that the surgeon might not be in so much of a hurry to operate and that he would not take the cecum out if it were due to protrusion of the valve.

in the region of the cecum at the time of admission.

There are a great many other things that might explain the local picture in this region. This woman had had no history of bleeding from the bowel. She was free from anemia—as a matter of fact she had 15.6 gm. of hemoglobin at entry, which is above normal. That brings up the question of tumors of the right bowel, which are supposed to cause anemia but which, as a matter of fact, only cause anemia in about 70 per cent of the cases. This could perfectly well have been a benign tumor, such as a lipoma, a lipofibroma or a true fibromyoma, or a benign polypoid lesion, although I strongly suspect that it was not of that type because she came to the hospital following an acute episode. This type of tumor does not cause an acute episode, except for intussusception, which does not permit a patient to stay in bed eighteen days prior to admission to the hospital; but an inflammatory lesion such as appendicitis could. That also could produce a defect similar to the one that we see here, but if the defect were still present from such cause I should expect that there would still be some leukocytic elevation, some elevation of temperature and some obvious tenderness in this region. Besides, in this film one sees a perfectly normal appendix. So I shall rule out appendicitis. Occasionally a single diverticulum of the intestine with diverticulitis occurs in this site. These cases produce symptoms and signs of acute appendicitis and are always diagnosed acute appendicitis preoperatively. The history is usually shorter than this and associated with a perfectly typical febrile reaction and a tender inflammatory mass. Therefore, I shall rule that out.

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diseases on the part of a better nourished population

To the medical profession much of the information in this report merely confirms what it well knows—that Boston continues to have an ably administered Health Department. A greater value, and one that the *Journal* hails, is that the report will be read in circles not usually reached by medical publications, and will take information on public health to places where it would not otherwise have been carried.

MEDICAL EPONYM

NEUFELD METHOD

A note on the observation of specific capsular swelling of pneumococci by Ferdinand Neufeld (b 1869) first appeared in *Zeitschrift für Hygiene und Infektionskrankheiten* (40 54-72, 1902) under the title 'Über die Agglutination der Pneumokokken und über die Theorien der Agglutination [Agglutination of Pneumococci, and Theories of Agglutination]' A portion of the translation from page 57 follows

If we mix equal parts of agglutinating serum and a bouillon culture of pneumococci, whether in the test tube or by intimate admixture on a coverslip of a loopful each of serum and culture, we observe in the hanging drop preparation distinct signs of swelling which in the case of a strongly potent serum appear immediately or after only a few minutes. The individual cocci swell up twice or three times their [normal] size and at the same time flatten out at their points of contact with each other, which are ordinarily pointed and their whole contour becomes indistinct and hazy.

Twenty nine years later, in an article with R. Ettinger-Tulczynska entitled "Nasale Pneumokokkeninfektionen und Pneumokokkenkeimträger im Tierversuch [Nasal Pneumococcal Infections and Pneumococcus Carriers in Animal Experiments]" which appeared in the same journal (112 492-526 1931), Professor Neufeld describes the inoculation of bouillon with nasal secretion. A portion of the translation from page 495 follows

The serum bouillon growth usually does not show a pure culture of pneumococci but a mixture of various bacteria (among them frequently, streptococci). Notwithstanding it is possible quickly and with certainty to identify typical pneumococci if advantage is taken of the fact that they promptly swell markedly in homologous rabbit (not horse!) serum.

And in a footnote on page 496 he observes

The swelling phenomenon has furthermore proved its worth to us as a simpler and more reliable means of typing pneumococci than the usual agglutination method.

R W B

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

THE PHYSICIAN'S ROLE IN TUBERCULOSIS CASE FINDING IN INDUSTRY

Some Massachusetts physicians have received a letter from the Division of Tuberculosis stating that significant findings were noted in an x ray film of the doctor's patient during an industrial survey of the plant where the patient is employed. A report of the x ray findings is given together with the information that the employee has been notified to consult his family physician so they may talk over the results of the report.

Routine x ray examination of the chest for the purpose of finding unsuspected pulmonary tuberculosis in apparently healthy people is not only being used in the induction centers for the Army and Navy, but also in pre employment examination in large industries and in the case finding programs of state health departments and the United States Public Health Service.

Efficiency of the x-ray There is no question that the x ray method is the most effective single means for finding unsuspected pulmonary tuberculosis. Its value is limited only by the extent to which it is used. A person may have pulmonary tuberculosis in any stage of the disease either without any symptoms or with symptoms that are not alarming enough to cause him to seek medical advice. In early cases of tuberculosis, the x ray evidence may be present three to five years before the disease has progressed to the symptomatic stage.

The absence of symptoms does not mean that the disease is not in an infective stage. In a recent study of 160 Army rejectees for pulmonary tuberculosis at the Middlesex County Sanatorium, it was found that only 10 of these had been previously known to have tuberculosis, and all were classed 1A by their local draft boards. By stage of disease, these cases were 75 per cent minimal, 14 per cent moderately advanced and 11 per cent advanced. The most significant fact from the public health point of view is that over half the patients with moderately advanced and advanced cases had positive sputums, and even 8 per cent of those with minimal cases had positive sputums. Such unsuspected bacillary cases are continuously seeding their communities with tuberculosis and must be found and segregated if tuberculosis is to be eliminated or reduced to a low level.

New program of case finding In order to pick up these undiagnosed cases the Massachusetts De-

partment of Public Health, in co-operation with the Massachusetts Tuberculosis League, inaugurated a program of pulmonary tuberculosis case-finding in industry on September 28, 1943. His Excellency, Governor Leverett Saltonstall, was the first to have an x-ray film of his chest, and he was followed by the State House employees. The x-raying is accomplished by means of a fully equipped mobile unit which takes a 4-by-10-inch stereoscopic photofluorogram at a cost of only 6 cents per film. The unit was purchased by the Christmas-Seal-supported tuberculosis associations of Massachusetts and is loaned to the department. X-ray surveys are conducted in industry on a voluntary basis and at the invitation of the plant management.

Follow-up of suspects. On the identification blanks that are being used, the employee is asked to name the physician to whom he wishes his x-ray report to be sent. If the x-ray findings are significant, a written report is sent to the physician and the employee notified by mail to see his doctor. It is hoped that when the latter presents himself to his physician for interpretation of the x-ray findings, he will be placed under careful clinical, laboratory and further x-ray studies to confirm or deny the impression gained from the first roentgenogram. If the diagnosis of pulmonary tuberculosis is confirmed, the physician should then report the case to the local board of health.

It is the responsibility of the district health officer to see that the employee found to have suspected tuberculosis presents himself to his physician for further studies and, if the diagnosis is confirmed, that the case is reported to the local board of health in the prescribed manner.

COMMUNICABLE DISEASES
IN MASSACHUSETTS FOR NOVEMBER, 1943

DISEASES	RÉSUMÉ		
	NOVEMBER 1943	NOVEMBER 1942	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	25	2	4
Chicken pox	1282	969	969
Diphtheria	31	5	14
Dog bite	600	564	598
Dysentery, bacillary	22	30	30
German measles	64	61	39
Gonorrhea	510	378	421
Measles	816	1073	597
Meningitis, meningococcal	44	12	8
Meningitis, other forms	9	6	•
Meningitis, undetermined	7	1	•
Mumps	398	639	358
Pneumonia, lobar	224	233	269
Salmonella infections	7	7	5
Scarlet fever	707	882	493
Syphilis	617	535	469
Tuberculosis, pulmonary	247	220	220
Tuberculosis, other forms	22	17	23
Typhoid fever	3	0	6
Undulant fever	6	0	5
Whooping cough	407	952	710

*Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

COMMENT

Anterior poliomyelitis, as might be expected, is now definitely on the downward grade. The meningococcal meningitis figure has remained in the forties for the last

four months. This is a decidedly high level compared with that of other years. Diphtheria has been creeping up since August; the November figure is the highest for this month since 1935, but this year's total probably will not exceed that of last year. Whooping cough, on the other hand, shows a 50 per cent decline over last November.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Actinomycosis was reported from: Springfield, 1; total, 1.

Anterior poliomyelitis was reported from: Adams, 2; Beverly, 2; Boston, 4; Cambridge, 1; Danvers, 1; Fall River, 3; Haverhill, 1; Lynn, 3; Natick, 1; New Bedford, 1; North Adams, 1; Norwood, 1; Pittsfield, 1; Saugus, 1; Seekonk, 1; Watertown, 1; total, 25.

Diphtheria was reported from: Boston, 12; Cambridge, 1; Chelsea, 1; Foxboro, 1; Gloucester, 1; Lowell, 4; New Bedford, 3; Salem, 1; Somerville, 4; Woburn, 3; total, 31.

Dysentery, bacillary, was reported from: Boston, 6; Brookline, 1; Cambridge, 2; Canton, 1; Hingham, 1; Ipswich, 1; Lowell, 4; Malden, 2; Melrose, 1; Quincy, 1; Stoneham, 1; Wellesley, 1; total, 22.

Encephalitis, infectious, was reported from: Braintree, 1; Brockton, 1; Fort Devens, 1; total, 3.

Malaria was reported from: Falmouth, 1; Fort Banks, 13; Fort Devens, 11; total, 25.

Meningitis, meningococcal, was reported from: Agawam, 1; Boston, 7; Brockton, 1; Cambridge, 1; Fall River, 5; Fitchburg, 2; Fort Banks, 1; Fort Devens, 1; Haverhill, 1; Holbrook, 1; Holden, 1; Leominster, 1; Lowell, 1; Lynn, 2; New Bedford, 1; Norwood, 1; Revere, 1; Saugus, 1; Somerville, 3; Southbridge, 1; Springfield, 2; Waltham, 1; Weymouth, 1; Worcester, 6; total, 44.

Meningitis, other forms, was reported from: Boston, 1; Holyoke, 1; Lawrence, 1; Malden, 1; Medford, 1; Milford, 1; Somerville, 1; Springfield, 1; Worcester, 1; total, 9.

Meningitis, undetermined, was reported from: Boston, 3; Cambridge, 3; Leominster, 1; total, 7.

Salmonella infections were reported from: Boston, 1; Cambridge, 2; Marblehead, 2; Wellesley, 2; total, 7.

Septic sore throat was reported from: Boston, 6; Clinton, 1; Malden, 1; Marion, 2; Milton, 1; New Bedford, 1; total, 12.

Trichinosis was reported from: Newton, 1; total, 1.

Typhoid fever was reported from: Lowell, 1; Malden, 1; North Attleboro, 1; total, 3.

Typhus fever was reported from: Williamstown, 1; total, 1.

Undulant fever was reported from: Dartmouth, 1; Easton, 2; Framingham, 1; Somerville, 1; Wareham, 1; total, 6.

CONSULTATION CLINICS FOR CRIPPLED
CHILDREN IN MASSACHUSETTS UNDER
THE PROVISIONS OF THE SOCIAL
SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Salem	January 3	Paul W. Hugenberger
Haverhill	January 5	William T. Green
Lowell	January 7	Albert H. Brewster
Brockton	January 13	George W. Van Gorder
Pittsfield	January 17	Frank A. Slowick
Springfield	January 19	Garry deN. Hough, Jr.
Worcester	January 21	John W. O'Meara
Fall River	January 24	Eugene A. McCarthy
Hyannis	January 25	Paul L. Norton

WAR ACTIVITIES

CIVILIAN DEFENSE

OCD AFFILIATED UNITS

The United States Office of Civilian Defense has recently announced that ninety-three hospitals and medical schools scattered throughout the country have completed the formation of affiliated units of civilian physicians, which will be available to either OCD or the Army in the event of need for setting up emergency hospital facilities in their respective areas.

Each unit is composed of fifteen physicians, surgeons and other specialists and forms a balanced professional staff. OCD will use the units to supplement the staffs of emergency base hospitals located in relatively safe zones on the fringes of critical areas in case it is necessary to transfer civilian patients to these hospitals because of emergency in such areas. Furthermore, the units will be called on by the War Department to staff externalized hospitals should there be a sudden influx of battle-front casualties, or some other extraordinary military necessity, requiring hospitals and physicians beyond the immediate capacity of the Army in any particular locality. The affiliated units will be used for military emergency purposes only in or near the communities in which the staff resides. Their duties will be temporary and they will be replaced by Army medical officers as quickly as the Surgeon General of the Army can make the necessary assignments.

Normally, the fifteen doctors of a unit are associated with a single hospital. Each unit includes a chief and assistant chief of medical services, two general internists, a chief and assistant chief of surgical services, four general surgeons, two orthopedic surgeons, one dental surgeon, one pathologist and one radiologist. Physicians accepted for service in the units receive inactive reserve commissions in the United States Public Health Service, but will be called to active duty by the Surgeon General (USPHS) only at the request of OCD. When a unit is needed either to staff an emergency base hospital or to assist the Army temporarily in a military emergency, the physicians of the unit will be placed on active duty for the duration of that particular emergency.

Following is a list of units completed and commissioned by the Public Health Service up to October 30, 1943, in Region I, which includes all the New England States:

Boston University School of Medicine Boston
Cambridge Hospital Cambridge Mass
Goodard Hospital Brockton Mass
Harvard Medical School (A) Boston
St. Luke's Hospital Pittsfield Mass
Springfield Hospital Springfield Mass
Central Maine General Hospital Lewiston Maine
Eastern Maine General Hospital Bangor Maine
Maine General Hospital Portland Maine
Elliot Hospital Manchester New Hampshire
Lawrence and Memorial Associated Hospitals New London Conn
Meriden Hospital Meriden Conn
Stamford Hospital Stamford Conn
Waterbury Hospital Waterbury Conn
Yale University School of Medicine New Haven Conn
Rhode Island Hospital Providence Rhode Island
St. Joseph's Hospital Providence Rhode Island

MISCELLANY

CANCER OF THE LUNG— A GROWING PROBLEM

Until recently, primary carcinoma of the lung was regarded as a relatively rare type of cancer. We are now

recognizing that it is one of the commonest forms of neoplasm. It has been discovered that around 10 per cent of all cancers originate in the lung, that this organ is surpassed only by the stomach as the most frequent site of beginning malignancy, and that approximately 15,000 Americans succumb annually to carcinomas that arise from lung structures usually in the bronchi. Such stark statistics and the demonstrated fact that cancer of the lung like pulmonary tuberculosis can be found early by employment of readily available diagnostic facilities, provide all physicians with food for thought as they evaluate the chest complaints presented by patients, especially men and particularly those past forty years of age. Many of the pertinent points are discussed in a recent paper (Overholt, R. H. A common masquerading lung disease *Dis. of Chest* 9 197-210, 1943).

There is a masquerading lung disease which often gives quarter for a short time before the fatal issue and whose actions, in many ways, may simulate those of tuberculosis.

Both diseases are unique for they masquerade as other acute or chronic conditions of the lung. In neither are symptoms reliable in the early stages. Both diseases are marked by a lack of early reliable physical signs. Both are unique since in the early stages a single x-ray film will usually show some abnormality. Again, they are one and the other because in spite of obscure clinical factors the diagnosis can be accurately made in a high percentage of cases. Lastly, there is a similarity between tuberculosis and this masquerading disease: cancer of the lung is successful treatment depends to such a large degree on early discovery.

However, the two diseases are different as regards the predominant age groups affected. Tuberculosis concerns principally the age groups between fifteen and forty, whereas lung cancer usually affects those between the ages of forty and sixty-five. The diseases are totally different in respect to the matter of time. In tuberculosis, time plus rest is often a useful ally of the patient in regaining health. In cancer of the lung the element of time is always an enemy of the patient. Prolonged observation and rest treatment never improve the situation, but rob the patient of his only chance for possible cure.

In 165 cases of lung cancer it was found that the patients first consulted a doctor because of symptoms usually associated with almost any chronic chest condition. A review of these symptoms suggests it would be impossible to set apart any group of complaints that could be regarded as pathognomonic of pulmonary malignancy. Nevertheless, 82 per cent of all the patients reported chronic cough, whereas no less than 92 per cent had as a first symptom something that called for attention to be directed to the chest when first the physician was consulted. Besides cough, other common symptoms included chest pain, chills and fever, hemoptysis, dyspnea, loss of weight and weakness.

Reviewing the physical signs elicited it is again impossible to outline a specific and significant grouping any more suggestive of cancer than of other chronic pulmonary conditions. Cases examined in the early stages often presented no physical signs. When present, the signs were of considerable variety and frequently misleading. They included evidence of congestion, consolidation, fluid localized emphysema, cavitation, bronchial obstruction, mediastinal shift and other phenomena varying with the case, thus emphasizing the unreliability of simple physical signs in the differential diagnosis of this condition.

Of the 165 cases, 104 (63 per cent) were incorrectly diagnosed by the first doctor consulted. In view of the confused picture of misleading symptoms and physical findings, perhaps this majority in favor of error is not completely surprising, but the sobering thought emerges that treatment based on an erroneous diagnosis was maintained for long periods of time, aimed at such supposed conditions as tuberculosis, 40 cases; unresolved pneumonia, 18 cases; lung abscess, 13 cases; bronchitis, 11 cases; asthma, 5; heart disease, 4; pleurisy, 4; metastatic tumors, 2; and miscellaneous, 9 cases. The most notable fact was the high frequency of false diagnoses of tuberculosis.

Unfortunately, lung cancer was not unmasked in far too many cases until long after the patient first visited a physician. It was possible in the case histories of 125 patients to determine how speedily a verified diagnosis was reached. Two facts stood out boldly. First, 36 per cent of the patients placed themselves under medical supervision at onset or within one month of the onset of symptoms. Second, the average patient consulted a doctor within three months of onset but did not receive benefit of a chest x-ray film for an additional three months. The true diagnosis was not arrived at until nine months had elapsed from the time when the first doctor saw the patient.

The x-ray, without doubt, is by far the most valuable aid in apprehending pulmonary disease, but a distinction is necessary between its ability to yield presumptive and absolute evidence. In 98 per cent of this series of cases the initial film revealed that trouble was present. An explanation of the delay in reaching a final diagnosis may be found in the fact that in the majority of cases the primary pathologic process failed to produce on the film or the fluoroscopic screen a shadow of itself. Those abnormalities that did appear were secondary effects due to the presence of the neoplasm and were of such variability as to be susceptible of a wide range of interpretation.

In 95 per cent of the cases it was possible to establish an unequivocal diagnosis during life, bronchoscopy being the leading method of obtaining tissue, and having been employed in 103 cases. In 39 other cases surgical exploration was used. Metastases were sectioned in a few cases, aspiration was the method in another small group, whereas the remaining 5 per cent were diagnosed only after post-mortem examination.

For a decade, surgery has been available in the treatment of lung cancer. A creditable showing has been made during this pioneering period. For example, 2 out of every 5 cases surgically explored have been found to be free of extension of the cancer extrapulmonarily. In 20 per cent of the entire group of verified cases there was some hope of cure. This seems an encouraging ratio when we recall that prior to 1933 there was no reason to regard the condition as anything but incurable. As a reward for our efforts, 20 patients, or 13 per cent, remain as the net salvage from the entire series of 156 verified cases of primary lung cancer, out of 32 selected for an attempt at curative resection. These 20 patients are all reasonably well and devoid of evidence of metastatic disease, and 5 of them can be referred to as "cures" in so far as they have now passed the five-year mark.

In considering practical steps toward bringing cases of lung cancer to light during the curable stage we can

learn valuable lessons from the record on tuberculosis case finding. Physicians have been taught that if tuberculosis is to be discovered during its minimal stage it is not necessary to search for absent or insignificant symptoms and physical signs but to go immediately to the x-ray. The same can be said for the apprehension of early lung cancer.

How may the first doctor consulted set in motion this mechanism of early discovery? He may save valuable time for his patient if he remembers:

1. That cancer of the lung is now one of the most important diseases of the chest in patients within the age period from forty to sixty-five years, particularly in males.
 2. That many patients do seek help at a time when the lesion is still confined to the lung.
 3. That symptoms and signs are either lacking or misleading in the early stages.
 4. That the earliest lesions will in almost every case produce some telltale shadow on the x-ray film, and
 5. Finally, that there are two methods available for clinching the diagnosis: first, that the majority of lesions are visible bronchoscopically and accessible for biopsy, and second, that when the suspicion cannot be verified in this way, it is possible to explore the chest safely by surgical means, settle the diagnosis and carry out curative treatment if necessary.
- Reprinted from *Tuberculosis Abstracts* (December, 1943).

NOTICES

BOSTON COUNCIL OF SOCIAL AGENCIES

The following series of lectures covering the problem of alcoholism from various aspects will be given at Zero Marlborough Street, Boston, on Friday evenings at 7:30 p.m. They are sponsored by the Committee on Alcoholism of the Boston Council of Social Agencies.

January 7 — The Heredity of the Inebriate. Dr. E. M. Jellinek, associate professor of applied physiology, Yale University.

February 11 — Alcohol and Public Opinion. Dr. Dwight Anderson, director, public relations, Medical Society of the State of New York.

March 10 — Effects of Alcohol: The evidence of physiological experiments. Dr. Howard W. Haggard, director, Laboratory of Applied Physiology, Yale University.

April 7 — The Treatment of Chronic Alcoholism. Dr. Robert Fleming.

Plan of Treatment at the Washingtonian Hospital with Special Consideration of the Conditioned Reflex Treatment. Dr. Joseph Thimann.

May 12 — Alcoholism, Criminology, and Parole. Reuben L. Lurie, chairman, parole board, Massachusetts Department of Correction.

These lectures will be open to the public.

(Continued on page xii)

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THE RELATION OF PHYSICAL THERAPY TO ARTHRITIS*

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NEW YORK CITY

TO cover adequately the major medical problem of the relation of physical therapy to arthritis, with all the finesse in selection of physical therapy and in the technical understanding necessary for its proper application, would require a book, not a paper. Again, arthritis itself presents diverse types of cases. On the one hand, one sees a patient who is not too uncomfortable, with low-grade arthritic changes occurring later in life. He philosophically accepts his aches and pains, goes along "moving his bones," and so, by this subtle form of physical therapy, maintains his motility and suffers little. On the other hand, one sees another patient with a hypochondriacal tendency who cannot stand pain, slows up, and takes too much treatment, often of the wrong kind. He stiffens up and is soon semi-invalided mentally and physically. Lastly, there are the extremely malignant deforming types of arthritis. An extremely careful classification of arthritis has been formulated. Several types of the disease may exist in the same patient. Often differential classification in a given case can be only conjectured. Diagnosis, however, is imperative before treatment can be prescribed with any degree of assurance or prognosis can become possible. The diagnosis once made, certain routines become obvious.

GOVERNING FACTORS

The treatment of an arthritic patient cannot be entered on until certain other factors are considered. These are as follows:

Psychologic Status

Arthritic patients often develop an anxiety neurosis when they learn the diagnosis. The lay press and radio have been major factors in creating

a fear of being crippled to fix itself in their minds. They may be anxious because of the inability to carry on the ordinary responsibilities of life that to them is increasingly evident. Fear of complete and ultimate dependency worries and frightens them. This anxiety is often part of a vicious circle. Psychologic analysis in a series of arthritic patients has at least suggested that the hypotonic state that accompanies worry may be a factor influencing the progress of arthritis.

Mental depression is present in many arthritic patients owing to continuous nagging pain that the physician often cannot alleviate. Depression due to narrowing of the sphere of activity because of slowing up or pain is often seen. The patient fears the influence that his semi-invalidism may have on other members of his or her family. The inability of the husband to get about, the difficulty the wife has in taking care of her part of the family responsibilities ordinarily vested in her, are both extremely depressing and are likewise causes for anxiety.

The balance or stability of the patient must either enhance or handicap the physician's efforts in caring for him. He may not be able to stand pain, or may lose confidence in his physician, or the prescribed routine may be diverted by outside influence.

Pain and Disability

Pain and disability are the urgent and immediate reasons for the patient's consulting a physician. The latter must not take these lightly. Although long-range treatment may be indicated, something must be done at once for the pain and disability to lessen the prolonged need for the anodyne assistance that is immediately necessary.

Prognosis

The prognosis occupies a prominent place in the patient's thoughts, and some honest satisfaction must be given him as soon as the diagnosis is made

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and future portents can be estimated. The estimated stability of the patient determines to what detail it is wise to discuss the subject with him. Some member of the family, however, should be told the facts. The diagnosis will probably demand certain alterations in customary habits. Immediate or prolonged hospitalization, orthopedic care in deforming types, even surgical intervention in some others, may be necessary. Such arrangements as have to be made should be entered into tactfully.

The Patient as a Whole

The most important psychologic attributes have been mentioned. The age, life expectancy, metabolic level, food habits, usual employment and the presence of other constitutional ailments, such as a cardiac condition in rheumatic fever and the presence of hypertension, gall-bladder disease, complicating peripheral vascular disease, alcoholism existing with gout, and pelvic inflammatory disease or chronic prostatitis associated with specific arthritis all enter into the treatment of arthritis, and may well influence the advisability or limitation of physical therapy in a given case.

METHODS OF TREATMENT

The importance of physical therapy in relation to arthritis varies within wide limits. It is of the utmost value under certain conditions, but has little bearing in some arthritic patients. Some of the available methods of treatment will now be discussed.

Moist heat is the first and most universally applicable modality. Certain chronic arthritics may be said to "live in bathtubs." Such low-grade, general heating is nothing less than fever therapy.¹ A patient submerged in a bath at a tolerance temperature (110°F.) for twenty minutes develops an oral temperature of about 102°F. If he crawls into bed and insulates himself against heat loss, the resulting increased metabolism may cause the generation of one or two degrees more of heat.

Generalized heat in cases with multiple joint pains is most acceptable and of distinct therapeutic value.² Locally, all sorts of hot fomentations, soaks, whirlpool and paraffin baths and steam jets are universally available.³

Dry heat by means of hot pads, radiant-heat lamps, infrared applicators, diathermy and short-wave radiation are acceptable methods for local application.

Massage is a highly useful type of treatment. The importance of the technic, however, is not generally appreciated.⁴ How many physicians who have written an order for massage have taken the time to watch the procedure being carried out and so have realized how varied may

be the technics and effects of this form of treatment.

Passive movement, manipulative procedures and therapeutic exercises are likewise of great value in maintaining and restoring functional joint movement in the arthritic patient.

Rest and restriction of activity as therapeutic measures, although perhaps not usually considered as physical therapy, are absolute requisites at some stages of arthritis.

Many patients are advised to "sit in the sun." The routine of rest, heat and ultraviolet rays, associated with a complete change of environment, does much for an arthritic patient, especially if carried out in a dry climate. Often at spas, this is combined with hydrotherapeutic routines, with excellent results. Unfortunately, only a limited number of patients can afford such luxurious treatment.

Various electrical applications, notably galvanic iontophoresis, by which various drugs are introduced into the tissues by way of the skin, are sometimes indicated. Application of static electricity has a certain proved value in reducing the swelling present in arthritic inflammations.

The least expensive type of physical therapy, and an intensely valuable form, is exercise. Unfortunately, however, this involves home routines. As such, it requires much patience, time and perseverance on the part of the physician to see that such exercises are carried out.

CHOICE OF METHODS

With this armamentarium of physical therapy at hand, the next problem is for whom, when, where, how and to what extent and in what combinations, to use these modalities. The employment of any form of physical therapy in a case of arthritis represents an expenditure of energy by someone, and often requires special apparatus or a setup to make it available. Physical therapy is time consuming, and when done by paid personnel it is expensive. For these reasons, it should not be prescribed unless there are definite indications for its use.

Roughly stated, the indications for physical therapy in arthritis are as follows: to improve the general condition, to reduce joint swelling, to relieve pain, to improve function, and to preserve function and lessen deformity. It should not be used for its psychologic effect or as a sign to the patient that something is being done for him.

From the viewpoint of physical therapy, arthritic patients may be divided into six classes: those with rheumatic fever, septic arthritis, gonococcal arthritis, gouty arthritis, rheumatoid arthritis (atrophic) and osteoarthritis (hypertrophic). A.

discussion of each of these types will suggest the reasonable approach to the problems of the application of physical therapy in other miscellaneous cases. The treatment must always be individualized, and must be fitted to the needs according to the symptom complex that each case presents.

Rheumatic Fever

Patients with rheumatic fever are constitutionally ill. The cardia is threatened. Rest is paramount. Salicylates are indicated. Any physical therapy must be administered at the bedside. The extremely sensitive joints should be splinted⁵ to prevent jarring, pain and irritation and to offset the development of a deformity. A cradle with continuous low-grade heat and the gentle, persistent use of hot fomentations to affected joints are gratefully accepted by these sufferers. Their posture in bed has much to do with their comfort. As soon as joint sensitiveness becomes less acute, they should be encouraged to move their joints within the limits of moderate pain. When the temperature subsides and convalescence is established, extreme care in ambulation should be exercised and special care taken when the patients are placed on their feet. Slippers with heels, strapping of the feet or soft arch supports may be required. The patients should not be waited on too much during their convalescence, since their extreme lack of activity during the acute illness greatly depletes their muscular strength. They need as much voluntary exercise as ordinary guided activity will ordain to counteract the generalized atrophy present in their skeletal muscles.

Septic Arthritis

The cases with specific joint infections, such as tuberculous, post-traumatic, and other septic infections, are not physical-therapy problems until surgical care has rendered them fit for mobilization. Physical therapy instituted while wounds are draining, such as active movement with or without associated traction suspension and massage when the danger of spreading infection has passed, together with the use of radiant heat, will do much to hasten functional return by reducing swelling and preventing contractures. The early use of this procedure in infections of the hand has a pertinent industrial significance. In these cases the infection has probably also involved the tendon sheaths—fibrositis often accompanies the arthritis. Whirlpool baths, massage and passive motion should be carefully applied. Active exercises including functional types of occupational therapy⁶ speed up and amplify recovery.

Gonococcal Arthritis

The day of the rigidly ankylosed joint due to Neisserian infection has passed. Arthritic complications with gonorrhea have become far less frequent since the introduction of the sulfonamides. Occasional resistive cases do develop gonococcal joints. There are two methods of handling these, induced fever and diathermy.

Physically induced fever adequately given produces a dramatic result.⁷ If fever therapy is not available, diathermy may be given through and through the affected joint in the subacute stage, with positive passive manipulation of the joints. This is probably the one instance where the patient's sensibilities are to a large extent to be overlooked in giving passive motion. Massage and active exercises within the increasing range of movement will prevent an ankylosis from occurring in a joint, even though extreme clouding and loss of joint definition may be demonstrable on x-ray examination. The assumption is that the source of the infection as well as the affected joint receives adequate treatment.⁸

Gouty Arthritis

Dietary restriction, wet dressings, elevation, colchicine, salicylates, elimination and alkalinization represent the accepted forms of treatment of gouty arthritis.⁹ Patients with acute joints should be encouraged to move their joints within the limits of swelling and pain. Hot applications and exercise will in themselves do much to reduce the swelling. Local spraying with ethyl chloride, together with the institution of exercise, is one method of initiating such movement painlessly, and may be a means of encouraging the patient to observe the beneficial effect of active movement in enhancing the assimilation of joint fluid.¹⁰

If the static brush discharge is available, it may also be useful in reducing swelling in acute gout. The patient should be cautioned regarding the future regulation of his exercises when recovery is complete.

Rheumatoid Arthritis

Patients with rheumatoid arthritis are constitutionally ill. They represent that type of arthritis in which the greatest involvement is in the soft tissues, and consequently physical therapy can have a definitely beneficial effect if properly applied. Aside from the general care of rest, a high-calorie, high-vitamin diet and forced fluids, physical therapy can do much for these patients. How to bring this treatment to the patient and not drain his financial resources completely is one of the gravest physical-therapy problems. The difficulty is that these patients need much time-

consuming, carefully guided, often changed physical therapy, which becomes extremely expensive.

The undulating course that these cases pursue creates a constantly recurring problem. Gold salts in selected cases have proved helpful, although inconsistent in their effects.¹¹ Being a heavy metal, gold must be given under well-controlled conditions. This form of treatment is definitely not the answer to the rheumatoid-arthritis problem.

The patient with an acute case without deformity should be kept at rest in bed, without lavatory privileges if possible, even if the lower extremities are not the major involvement. If swelling of the joints of the lower extremities is present to any extent, bivalved casts should be applied to immobilize the extremities, lessen joint irritation, and relieve the pain attendant to being moved during nursing care. These casts should be formed with joints in position to offset the development of flexor contractions or eversion of the feet. If the hips are involved and adductor spasm is present, the thighs should be held in abduction of 45° with an arrangement for preventing external rotation of the thighs. Later, casts or caliper splints may be necessary for ambulation.⁵ If only the knees and ankles are involved, molded splints should be applied for immobilization. In cases with marked swelling of the upper extremities, molded splints on the forearms, wrists and hands to prevent flexion deformity, eversion at the wrists, and disalignment of the finger digits should be applied. With this immobilization, various forms of gentle heat may be tried and will often alleviate pain and hasten reduction in swelling. The heat must not be intense, or the pain and swelling may be aggravated. Patients should be impressed with the importance of elevation of the extremities in lessening edema and the importance of the early reduction of swelling.

Each day the extremities should be removed from the casts and passive motion within limits of pain be given. Active exercises when the sedimentation rate is above 35 mm. per minute is apt to cause an exacerbation of symptoms in a case in which there has been a previous recession. With a lowering of the sedimentation rate and a diminution in swelling and protective spasm, the patient may be given a stroking massage and a graduated exercise program may be instituted.

In the case of hips and shoulders, exercises under water, preferably in a large therapeutic tank in which the temperature may be elevated to 100 or 102°F., are helpful early in the exercise routine. Such tanks often provide whirlpool arrangements that, when directed to the painful joint, relieve pain and, with the buoyancy of the water, en-

courage active movement. When exercises are once begun, they must be progressively increased as regards effort and range, but kept within the limits of fatigue and pain.

Deep breathing and bed calisthenics for the general condition occupy a prominent place in such a routine. In bed, patients should be encouraged to do moderate exercises, often with the assistance of weight-and-pulley arrangements. Care must be exercised while these patients are bedridden to prevent the friction of linen at the elbows, heels and buttocks. Body radiation with ultraviolet rays¹² will assist in overcoming the secondary anemia present in these cases. Small transfusions may give a sharp boost to severely debilitated patients.

Ambulation, as in the case of rheumatic fever, must be carefully and progressively carried forward. Crutches, walkers, supporting casts and caliper braces on the knees all have their place in treatment. Persistent accumulation of fluid in the knees may indicate synovectomy before ambulation can be successfully carried out. Splints must be worn well into convalescence, at night and in periods of relaxation during the day.

The hands tend to flatten and lose their normal lateral flexibility. This is usually due to lack of movement at the metacarpocarpal articulations. Manipulation of the bones in this area may be necessary before mobilization of the palm can be effected.¹³ Fibrositis is usually present in the fingers if edema and swelling have been prolonged. This requires rigorous and at times painful treatment if it is to be successfully combated. Manipulation of the phalangeal joints once a week and active and passive exercises daily following hot applications form the method of choice.¹³

The removal of persistent edema about the wrists and ankles may be expedited by the use of the static-wave current if available. It may also be accomplished by mild graduated exercises made possible through the prevention of pain by an ethyl chloride spray or iontophoresis with novocain.¹⁴

To pass over the subject of rheumatoid arthritis without mention of Still's disease would be a grave omission. Treatment of these unfortunate children should stress the prevention of deformities due to joint destruction and flexion contracture. Progressive casts seem more logical than arrangements for suspension traction. A mechanical pull slightly misdirected or of too great intensity may produce abnormal angulations at the epiphyses of the long bones. Since investigating Kenny packs, I have discovered that intensive packing relieves pain, diminishes swelling, releases protective spasm, and prepares the patient

for the application of casts in a position of minimal deformity.

Patients with Strümpell-Marie arthritis should be kept on an exercise routine from the time the diagnosis is made. This should include thoracic and breathing exercises. By such care, ultimate deformity may be lessened. Radiotherapy has to date exerted the next most beneficial results in these cases.

Osteoarthritis

The large group of cases of osteoarthritis may be divided roughly into traumatic and metabolic. Some cases represent combinations of both, as in the trauma to the joints of the lower extremities and back that is present in fat, middle-aged patients. In the cases due to direct trauma to a joint or to fracture involving the joint surface, the success of the treatment depends on the institution of physical therapy as early as possible to reduce synovial accumulation, relieve pain, and permit active movement of the joint involved.¹³ The greatest factor in treatment is to prevent progressive fixation.

Deep heat, not too intense, is used to improve the circulation within the joint capsules and less penetrating forms of heat for reflex circulation and relaxation of the protective spasm. The heat applications available for this purpose range from hot soaks, contrast baths and other forms of hydrotherapy to paraffin baths, mud packs, electric pads and radiant-heat lamps.¹⁰ Exercises further reduce muscle spasm if they are done within the limits of pain and are properly directed and stepped up progressively along with increased flexibility in joint movement.

Pain comes with prolonged lack of movement and pressure on opposed joint surfaces where the cartilaginous insulation is gradually disappearing. This pain is lessened through activity if carried out without weight-bearing.

In certain areas, special problems present themselves for consideration in the treatment of the osteoarthritic patient.

Cervical arthritis often exists without any notable subjective symptoms. It may, however, be the cause of a diverse array of both subjective and objective symptoms based directly on the progressive pathologic changes taking place.

The earliest pathologic manifestation is a synovial irritation with a tendency to calcification at the ligamentous attachments to the vertebrae. This is followed by definite osteoarthritic lippling and the intrusion of new bone about the foramina through which pass the spinal nerves. A narrowing of the intervertebral spaces occurs, with mechanical condensation in the neck and poor mechanics of head carriage.

The symptoms produced are largely mechanical, with increasing limitation of range of movement of the neck. Pain, at first only on movement of the head and neck in certain positions, but later with pressure developing about the cervical nerves, is radicular in type. This pain is directly related to posturing of the neck, and segmental distribution of pain has reference to the anatomical distribution of the cervical nerves. Pain is often more pronounced on one side than on the other. It may simulate bursitis, myositis or the true neuritis so common to this area. Mild cervical bony disarrangements may give similar symptoms. An exact differential diagnosis must be made before prognosis or proper treatment can be instituted.

The application of physical therapy varies considerably with the diagnosis. In true cervical arthritis, diathermy, massage and graduated exercise are indicated. Manual traction or suspension¹⁷ accompanied by gentle rotation are helpful in overcoming the crowding of structures in the neck that occurs with pain, protective spasm, bony hypertrophy and thinning of the intervertebral disks. Marked thinning of but one disk with arthritic changes in the presence of a history of trauma or acute snapping of the neck may be the cause for further studies to eliminate disk herniation, with its surgical indication for laminectomy.

Arthritis in the thoracic spine may be the result of poor posture, often occupational. A wedging round back or structural scoliosis may be the cause. Early discovery of bad posture and its correction will do much to prevent arthritis. Spinal fusion in structural scoliosis in children should be considered to offset pain, disability and semi-invalidism on reaching young adulthood.

Arthritis in the thoracic spine in women is often complicated by the undue strain of supporting abnormally large, fat or pendulous breasts. In these cases, relief will be accelerated if a brassière is constructed that distributes the support of these structures more evenly over a larger area of the back and shoulders.

Osteoarthritis of the lumbar spine has to do with old strains and injuries, metabolic causes, altered mechanics of weight bearing in middle-aged persons due to abdominal adiposity and loss of tone in the back muscles because of lack of exercise. The arthritis may be superimposed on a spine with asymmetrical or oblique unstable facets, often involving several vertebrae. As in the cervical region, the differential diagnosis must be carefully made, since there is much to be considered before all the symptoms can be made to repose on an arthritic diagnosis. Time does not permit discussing the differential diagnoses possi-

ble in this area. It will suffice to recall the various cases constantly seen of traumatic strains, tuberculosis, carcinomatous metastasis, myositis, disk herniation, functional, structural or referred back pains, osteomalacia and spondylolisthesis.

The arthritis may be superimposed on or exist with some of these other conditions, and so the treatment must be made to fit the case. Some cases of lumbar arthritis require mobilization. In others this is contraindicated or is advisable only after the acute symptoms have subsided. In structurally weak backs, exercise aggravates the symptoms. A period of limitation of movement may be advisable with curtailment of activities, even of golf playing, which delivers much torsion strain to the lumbar and lower dorsal spine. The age of the patient, the extent of the arthritis, the amount of thinning of the disk or of flexibility retained in the back and the presence of other complications, together with experience, are guides to the proper advising of these patients. As mentioned previously, however, efforts to increase the functional motility of the arthritic joints should be carried out, provided no apparent contraindication exists. Marked arthritic hypertrophic changes and marked thinning of a disk or disks should be considered as absolute contraindications to passive manipulations of the lumbar spine or straight leg-raising exercises.

In arthritis of the lumbar spine, obesity must be treated when present. High back corsets or braces with inclusion of arrangements for abdominal support must be given to stout patients with abdominal sag. It is impossible to relieve back pain until this weight has been taken away from an overburdened, acutely angulated lumbosacral joint and distributed over a wider longitudinal area of the back. Heat, massage, static electricity, exercise, a flat or firm bed, and supports are the forms of physical therapy indicated.

Consideration of *arthritis of the legs and of the knees and ankles* always involves the problem of supporting superimposed weight. Limitation of the patient's sphere of activity is another problem. These patients must all be treated as potential invalids, and every prophylactic means should be employed to prevent such a catastrophe. A few considerations are weight reduction to lessen the load and the early use of crutches to assist in weight-bearing, especially when synovial irritation is acute. Patients with mild symptoms do not relish being advised to wear crutches. Nevertheless crutches if used early are most valuable. The use of canes throws too much strain on the wrist and elbow joints, and the canes are often not of proper length, causing the patient to walk in the position of hip and lumbar-spine flexion. Also, canes tend to encourage the development of

flexion deformity, and often reactivate an arthritic lumbar spine. A general limitation in weight-bearing, with rest off the feet for a fixed period each day, should be advised.

These patients get much relief from diathermy applied directly through the hip joint, massage,—especially to the adductors of the thigh,—exercises to be done by the patient at home at least two times daily, and passive stretching of the hip joint and fascia of the thigh to maintain as much motion as possible. It should be explained to patients with rheumatoid arthritis or osteoarthritis that physical therapy is not going to cure their arthritis but that a course of physical therapy periodically will do much to make possible the maintenance of their activities. As soon as the patient's symptoms permit, physical therapy should become less frequent and should eventually be stopped entirely in favor of home routines, to prevent the patient from depending too much on such treatment.

The possibility of performing a hip fusion in cases with extreme degeneration should be kept in mind. Such an operation, provided the lumbar spine is flexible, leaves the patient quite capable of attending to any of his normal duties and, if successfully completed, removes the constant pain such patients suffer.

Arthroplasty of the hip by the Smith-Petersen¹⁸ method or variations of this procedure may offer the patient a chance of hip function when the restriction of movement is extremely advanced, although the results of this operation have been disappointing in some series of cases. The success of the procedure depends entirely on the use of physical therapy as soon as possible postoperatively along the lines recommended by Smith-Petersen. Unless the patient has sufficient fortitude to tolerate some pain during this period, he himself may ruin an otherwise skillfully performed operative procedure.

The use of any mechanical device that will prevent the pain of weight-bearing is indicated in the care of an arthritic patient.

Traumatic arthritis of the cuneiform navicular articulation is commonly seen in heavy, flabby patients, both young and old. These cases require foot support in addition to physical therapy. If these methods do not reduce the pain of weight-bearing, the patient may require orthopedic surgery until walking becomes less of an ordeal.

SUMMARY AND CONCLUSIONS

Physical therapy has a distinct place in the treatment of various forms of arthritis.

The use of physical therapy is varied with different types and in different stages of arthritis.

When physical therapy is prescribed, the routine should be rational.

Physical therapy should not be promiscuously prescribed or be continued indefinitely when prescribed.

The actual physical therapy must be done by skilled technicians who are familiar with the disease that they are treating.

Care should be taken that the patient does not get a false impression that physical therapy will cure his arthritis, except in the case of Neisserian arthritis.

Injudicious physical therapy may be a large factor in complicating an arthritis with a superimposed neurosis.

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COEXISTING INTRAUTERINE AND EXTRAUTERINE PREGNANCIES*

A Review with the Report of a Case

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THIS paper was prompted by the occurrence in my experience of an obstetric situation that need not be considered a rarity but that may be regarded as an unusual combination—namely, the coexistence of an extrauterine with an intrauterine pregnancy. The extrauterine aspect itself was typical in detail to that of any other pregnancy occurring within a fallopian tube and therein developing to the stage when the symptoms and signs suggested internal hemorrhage, and possibly tubal rupture, making prompt surgical therapy imperative. The other feature—that is, the intrauterine pregnancy—by itself was also completely normal in that the prenatal course, after the above surgery, was uneventful and that a simple, in fact precipitous, pelvic delivery of a normal female infant occurred. The unusual aspect was the coexistence of the extrauterine and intrauterine pregnancies, each having been treated separately, with a living infant resulting from the intrauterine implantation.

CASE REPORT

Mrs. H., a 33-year-old quartipara, consulted me on February 12, 1942, because of vaginal spotting and an associated persistent but slight pain in the right lower abdomen.

men for 5 days. Ordinarily the menstrual periods occurred every 28 days, lasting for about 5 days without pain and with an average flow. The last normal catamenia had occurred on December 20 to 25, 1941. The previous pregnancies were all normal except the fourth, which occurred in 1939. This pregnancy produced symptoms much like her current apparent gestation and was diagnosed elsewhere as a tubal pregnancy. She was not operated on, however, and at 5 months she miscarried. She had had no operations or serious illnesses, and there was no family history of multiple pregnancy.

Physical examination revealed a somewhat thin, palish woman. The temperature was 98°F., the pulse 80, the blood pressure 125/75, and the weight 102 pounds (the average nonpregnant weight was 100 pounds). There was slight tenderness in the right lower quadrant of the abdomen, and a detectable mass the size of an orange was palpated just above the symphysis, which was assumed to be a pregnant uterus. A differential diagnosis of threatened abortion, appendicitis or tubal pregnancy was considered, with the first thought the likeliest. The patient was put to bed under observation, with conservative treatment.

On February 23, the patient had sudden, severe pain in the right lower quadrant, which persisted. The vaginal spotting had neither disappeared nor increased. There was no elevation of temperature, the pulse was 100 and was of good quality, and the abdomen, especially in the right lower area, was markedly tender both by palpation and by rectal examination. Although the only palpable mass was the one in the lower midline, a diagnosis of ectopic pregnancy with hemorrhage and possible tubal rupture was tentatively made and the patient was hospitalized.

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Blood studies showed a red-cell count of 3,100,000, with a hemoglobin of 9 gm. (Sahli), or 58 per cent, and a white-cell count of 7200, with 65 per cent neutrophils. Urinalysis of a noncatheterized specimen was negative except for the slightest possible trace of albumin and occasional white blood and epithelial cells. Although the surgical consultant and I agreed concerning the probable diagnosis of tubal pregnancy, we were unable to account for the lower midline mass, the size of a large orange and itself nontender, except that it was possibly a pregnant uterus in the process of aborting. The patient was closely observed for another 15 hours, at the end of which time, there being no essential change, an exploratory laparotomy was done. The report of the surgeon was as follows:

A lower median incision revealed a bluish-appearing peritoneum, which when opened showed many old blood clots and a mass in the right pelvic region consisting of a tubal pregnancy. This had apparently bled through the fimbriated end of the tube but showed no evidence of rupture. The entire right tube was removed. The left tube was cystic and was also removed. Both ovaries appeared normal. The uterus was about the size of a 3-month pregnancy. The appendix was small and cordlike, with firm adhesions holding down the terminal third, which was freed. The appendix was removed in the usual manner, the stump was buried, and the wound was closed tightly in anatomical layers after inserting about a pint of normal saline solution in the peritoneal cavity.

The report of the pathologist was as follows:

Three specimens were received. The first consists of a fallopian tube, 10 cm. long and swollen to a diameter of 4 cm. in its proximal third. It is deeply congested and tense but intact. Section shows that the patent portion is filled with blood, but that the swollen portion is occupied by a swollen deep-red mass oozing blood when cut, which in its center has a tiny sac filled with clear fluid and showing a 3-mm. fetus. Soft, blood clots are adherent to the fimbriated end. The second is a small tortuous fallopian tube showing some congestion. The third is an appendix 5 cm. long and 4 mm. wide, with a little fat attached to it; on section there is thickening of the walls with partial occlusion. *Gross diagnoses:* tubal pregnancy (unruptured), fallopian tube and healed appendicitis.

On microscopical examination the first fallopian tube shows some thinning of the wall and plicae, with capillary engorgement, which appears to be a pressure phenomenon due to the presence of considerable fresh blood, as well as chorionic villi, in the lumen; the serosal vessels also show engorgement. In the second fallopian tube there is thickening of the walls and plicae, accompanied by vascular engorgement and lymphatic infiltration. The appendix shows marked fibrous proliferation of the submucosa, with replacement of the lymphoid tissue and mucosa and obliteration of the lumen. *Microscopic diagnoses:* tubal pregnancy, chronic salpingitis and healed appendicitis, with obliteration of the lumen.

Although both the surgeon and I commented on the uterine enlargement, we assumed that such enlargement was concomitant with the ectopic pregnancy. The patient had an uneventful recovery and was discharged from the hospital on the 13th day.

Several weeks later, the patient's husband stated that she was doing well, carrying on her household duties, but that she was "bloating." He was urged to bring her to the office for a complete checkup, but this was not done until August 6, or 5 months after the operation and 7½ months after the last normal menstrual period.

Examination at that time showed the weight to be 109 pounds (the most that the patient had weighed during her previous pregnancies was 115 pounds). There was no detectable edema. The urine was essentially negative and the circulatory system showed evidence of good function. However, there was a mass in the abdomen that extended slightly above the umbilicus, and a fetal heart rate of 140 was detected in the left lower quadrant of the abdomen. A uterine pregnancy, apparently the second half of a combined intrauterine and extrauterine pregnancy, was diagnosed. With the last normal catamenia occurring on December 20, 1941, the patient was told that her probable date of confinement was September 27, 1942. Owing to transportation problems she was unable to return for further prenatal observation, but on August 15 her husband reported that the membranes had ruptured, with the escape of 1000 cc. of fluid. He was advised to report further if labor commenced or if further symptoms developed. Not until September 2, or approximately 2 weeks after rupture of the membranes, did definite labor commence. The patient was then hospitalized, and 4 hours later, after variable pains, she spontaneously delivered a normal 4-pound, 6-ounce female infant before she could be transferred from the labor to the delivery room. The post-partum courses of the mother and baby were normal in every respect.

This case illustrates combined intrauterine and extrauterine pregnancies in which an early bleeding, nonruptured tubal gestation was treated by surgical removal and the intrauterine pregnancy proceeded to near term, with the pelvic delivery of a slightly premature but normal infant, who survived. This case and others like it suggest several practical points in the diagnosis and management of such an obstetric situation.

First of all, the lives of the mother and of the intrauterine fetus are particularly dependent on the correct treatment of the extrauterine aspect. Thus, in early prenatal care when the mother complains of pain in either vault, the physician in his differential diagnosis should consider not only the commoner types of pelvic disease, appendicitis and so forth, but also the possibility of extrauterine pregnancy. In a fair proportion of patients with this condition, there is no vaginal bleeding or spotting but evidence of internal hemorrhage. When once diagnosed in early gestation, an extrauterine pregnancy should be terminated forthwith by surgical means.

On the other hand, when a patient presents herself primarily with the clinical picture of an early ectopic pregnancy, irrespective of its activity, she should also be considered as a candidate for combined intrauterine and extrauterine pregnancies. This is especially true if there is a family or

personal history of multiple pregnancy. Although the diagnosis of an associated intrauterine pregnancy is oftener than not overlooked or not thought of, there is one common finding — namely, a uterus whose size and consistence as felt preoperatively and as seen and felt during laparotomy suggest that it carries a fetus. It is true that hypertrophy and hyperemia are also evident in a non-pregnant uterus associated with an extrauterine gestation, but to a less extent. In this case, the enlarged uterus as felt preoperatively was largely responsible for the period of conservative treatment, since a threatened abortion could not be ruled out. Because both the amount of hemorrhage and the surgical trauma are probable factors in precipitating a spontaneous evacuation of the intrauterine contents, early diagnosis prior to much hemorrhage and surgical treatment with minimal trauma are helpful in saving the intrauterine fetus.

DISCUSSION

Definition of Terms

Coexisting intrauterine and extrauterine pregnancies may properly be subdivided into two groups: combined or simultaneous; and compound. Much of the literature has failed to differentiate these types.

In the compound type the intrauterine pregnancy becomes superimposed on an already existing extrauterine implantation. The latter may have been present for a variable time and in some cases for several years. As a rule the extrauterine pregnancy of this category is quiescent and nonproductive of symptoms but may be detected by physical examination. It may exist in a chemically altered state ranging from saponification to mummification or to calcification or the lithopedion stage. Repeated intrauterine implantations with normal development to term may be superimposed on an existing dormant extrauterine pregnancy. The quiescent extrauterine product of conception may be discovered during a normal intrauterine pregnancy when a prenatal or postpartum examination discloses an unexplained mass, or at operation for a suspected abdominal neoplasm, or during the post-mortem examination of a patient whose death may have been due to an unrelated cause.

Combined intrauterine and extrauterine pregnancies, including the case reported above, present a different situation. This combination is probably identical with a multiple pregnancy except that instead of the implantations occurring normally within the uterine cavity, one or more of the fertilized ova reach the intrauterine spaces,

where they commence normal development, whereas the remaining one or more become simultaneously implanted outside the uterus — that is, in the fallopian tubes or in the ovary or at some site within the abdominal cavity. (The expression "one or more" is used because a limited number of cases have been reported where co-existing intrauterine and extrauterine pregnancies have occurred in which more than one fertilized ovum has become implanted either within or without the uterine cavity.) The extrauterine pregnancy may produce the typical symptoms and signs of early ectopic pregnancy at four to twelve weeks, usually at about eight weeks, when internal hemorrhage or tubal rupture occurs, suggesting the necessity of prompt surgical relief; or the extrauterine pregnancy may fail to cause the classic syndrome of the early weeks and proceed to develop to term or near term and even be productive of a viable, not necessarily normal, fetus. The intrauterine pregnancy of this combination, for the most part, is no different from any other such gestation; it may abort or miscarry, with or without apparent cause, or it may proceed to term with the delivery of a normal living infant.

Compound Type

The compound type generally lacks the dramatic character of the combined one because, as a rule, the extrauterine feature is dormant and nonproductive of symptoms. Moreover, the apparent rarity of compound intrauterine and extrauterine pregnancies is due not to the intrauterine aspect but rather to the scarcity or nondiscovery of an extrauterine product of conception of a kind to make this combination possible. There is apparently no physiologic or anatomic reason why a normal intrauterine pregnancy may not superimpose itself on an already existing dead or chemically changed extrauterine fetus and develop normally. Incidentally, the converse is not true; namely, there is no convincing evidence that an extrauterine pregnancy ever superimposes itself on an already existent intrauterine pregnancy.

Bland, Goldstein and Bolton¹ in 1933 stated that the calcified fetus was recognized as early as 1595, and they were able to collect an aggregate of 197 reported cases. Although all these cases with extrauterine products of conception did not at the same time produce normal intrauterine pregnancies, a fair number went through one or more full-term pregnancies resulting in the birth of healthy children without the extrauterine gestation's giving rise to difficulty. Bland and his associates report a case in which a mummified fetus was carried by a patient for fifteen years, and states that at operation this fetus showed evidence of having had developed approximately to the eighth

month. Moreover, the patient, prior to operation for the removal of the mummified fetus, had uneventfully passed through three full-term intrauterine pregnancies.

The quiescent extrauterine gestation may show various chemical alterations, dependent on its duration. Thus, there is first a saponification, then a drying-out process or mummification and finally the calcified stage. These changes obviously require considerable time and are without apparent clinical symptoms. Perusal of the literature fails to show evidence of endocrine imbalance owing to the presence of a quiescent extrauterine pregnancy.

Combined Type

The first report of combined intrauterine and extrauterine pregnancies was made by Duverney² in 1708. His observations were made post mortem on a patient who died of tubal rupture in the third month of pregnancy. In 1876, Parry³ stated that of 500 tubal pregnancies, 22 had combined extrauterine and intrauterine pregnancies. Marten and Meyer⁴ estimate the occurrence of combined intrauterine and extrauterine pregnancies as 1 in 105 ectopic pregnancies. Since 1 ectopic pregnancy occurs for approximately 300 normal pregnancies, the rough incidence of this combined type is apparent. Bernstein⁵ states that Strauss in 1898 had collected 32 cases of the combined type. From this date on, several authors summarized the literature, and in 1940 Bernstein, excluding the obvious compound type, collected 294 authentic cases. Ludwig⁶ in the same year collected a total of 353 cases, but he probably had not excluded the compound type. Of this number, 16 were diagnosed post mortem and of these all but 1 were recorded prior to 1897 or before the era of abdominal surgery.

Nonpregnant Uterine Changes in Association with Ectopic Pregnancy

An effort was made to correlate the changes apparent in the nonpregnant uterus with an associated ectopic pregnancy. Perusal of the literature leads one to the conclusion that the cervix softens and the uterus enlarges. Preoperative clinical examination in some cases of ectopic pregnancy failed to reveal evidence of definite uterine enlargement, but bimanual examination was not always satisfactory owing to obesity or to excessive abdominal tenderness. The increased size of the uterus, when detected, did not, however, equal the size to be expected if it were pregnant. In reports of cases in which the extrauterine pregnancy reached term (Woods,⁷ Hamblen⁸ and others), the nonpregnant uterus was generally no larger than a two-month pregnant uterus. Surgeons operating on ectopic pregnancies generally

report that the uterus is enlarged and soft but usually no larger than a two-month or two-and-a-half-month gestation, irrespective of the duration of the extrauterine aspect. In some cases the uterus is said to be normal in size.

DeLee⁹ summarizes this subject as follows:

In response to the stimulus of pregnancy the uterus hypertrophies, but not as much as it would if it were carrying the ovum itself, and it exhibits intermittent contractions. A decidua develops in it and this may be as much as 1 cm. in thickness, presenting all the characters of an intrauterine pregnancy decidua, except that it contains no chorionic villi. At the time of spurious labor or spurious abortion the decidua is cast off, either in one piece, as a cast of the uterine cavity or in large shreds or plaques, sometimes accompanied by feto. With death of the fetus the uterus shrinks.

When the uterus is definitely enlarged and irregular uterine hemorrhage occurs, it is suggested that an analysis of this discharge should be made for the presence of particles of tissue. The presence of decidual particles with complete absence of fetal villi indicates an ectopic pregnancy; the presence of both decidual particles and fetal villi indicates the abortion of a uterine pregnancy, with or without an associated extrauterine pregnancy.

Age, Parity and Multiplicity

Based on the reported cases, the maximum incidence of combined pregnancies, or 60 per cent, occurred in women from twenty-six to thirty-five years of age with a tendency to fall in the latter years. None are reported in mothers under twenty years of age, and 8 mothers were past forty-one years, with the oldest aged fifty-four. Multiparity tended to predispose to the condition, and of the 178 patients whose parity was known, 11 per cent were nulliparas and 89 per cent were multiparas, with biparas predominating. Six patients had previous multiple pregnancies; data in the published case reports pertaining to the family history of multiple pregnancies are incomplete.

Duration of Intrauterine Pregnancy

There are various important factors in the duration of intrauterine pregnancy. First of all, there is the group of patients, irrespective of extrauterine complications, who abort or miscarry from endocrine, physiologic or anatomic reasons. As part of the therapy associated with an abdominal operation for ectopic pregnancy the surgeon may do a dilatation and curettage, with or without knowledge of a possible intrauterine pregnancy. At least 6 cases in this series were so aborted. The influence of excessive intraperitoneal hemorrhage and of trauma incident to operation may enhance a spontaneous uterine evacuation. Of the 221

cases in which the duration of the intrauterine pregnancy was recorded, 92, or 35 per cent, terminated in the first trimester, 35 or 15 per cent in the second trimester, and 104 or 44 per cent, in the third trimester. Of the latter, 88, or 35 per cent, went to term.

Duration of Extrauterine Pregnancy

The duration of extrauterine pregnancy is recorded for 125 cases, of which 107, or 85 per cent, were terminated in the first trimester, with 56 so treated at eight weeks. Seven, or 6 per cent, were terminated in the second trimester and 11, or 9 per cent, in the third trimester, with 8 patients, or 6 per cent, going to term.

Diagnosis, Treatment and Mortality

If the condition was diagnosed early, the symptoms and signs were those of an ectopic pregnancy, if late, the picture was primarily that of an intrauterine pregnancy. Two hundred and nineteen cases, or 75 per cent, were diagnosed in the first half of pregnancy, with a total of 16 deaths, or a mortality of 7 per cent. Hemorrhage and peritonitis were the chief causes of death. Twenty cases were diagnosed in the second half of pregnancy, with 7 deaths, or a mortality of 35 per cent. This is the dangerous period. All the patients who died were operated on. The deaths were due to hemorrhage, septicemia, pulmonary embolism and pulmonary edema.

Operation during the late stage, although advised, involves certain technical considerations. Walling off, as in a cesarean section, is necessary in order to minimize the escape of amniotic fluid, if possible, because the fluid is an active peritoneal irritant. If the placenta is implanted on the broad ligament, it may be removed and possibly hemostasis effected without complications, but if the implantation is on the aorta, the liver or parts of the gastrointestinal tract, it seems wisest to cut the cord close to the placenta, leaving the secundines intact to resolve, as they promptly do if there is no infection. Institution of drainage is a matter to be decided in each case. If the fetus is dead, the secundines can be removed from any site without difficulty.

Thirty-six, or 12 per cent, of the cases were diagnosed at labor. About half of these had a mass so symptomless that no operation was done. Eight patients passed the fetus piecemeal through a fistula, and 1 of them died. The other half gave evidence of infection or intestinal irritation, or both. A live child was removed in 5 cases, one to twenty-three days after the intrauterine labor.

The maternal mortality of the whole series was 21 per cent, or 14 per cent if those cases are excluded in which the diagnosis was made post

mortem and the patients did not receive treatment. Fetal mortality from the intrauterine implantation was 54 per cent,—that is, 103 of the 226 fetuses survived,—whereas the fetal mortality from the extrauterine gestation was approximately 90 per cent, 11 of 215 fetuses surviving.

Extrauterine Fetal Abnormalities

The fetus that develops to term in an extrauterine pregnancy tends to have malformations, contractures, a flattened head and so forth. The reasons advanced for this are a scarcity of amniotic fluid, the lack of uterine protection, the pressure of surrounding structures and a concurrently developing uterus. Moore and Sile¹⁰ in 1870 reported the first case in which both extrauterine and intrauterine fetuses were delivered alive. An interesting case report is that of a Negress who simultaneously produced viable fetuses within and without the uterus.¹¹ She had a strongly positive Kahn reaction. The intrauterine infant had congenital syphilis, whereas the extrauterine one did not. The paternal history was not given. A few case reports include multiple pregnancies in which more than one fetus was present, either in the intrauterine or the extrauterine site.

SUMMARY AND CONCLUSIONS

An original case illustrating coexisting intrauterine and extrauterine pregnancies with appropriate treatment of each phase is reported and discussed.

A review of the literature covering both the compound and combined types of coexisting intrauterine and extrauterine pregnancies is given.

It is not so much the intrauterine aspect that makes this obstetric situation unusual as the coexisting extrauterine pregnancy. In the compound type the extrauterine pregnancy is quiescent whereas in the combined type the extrauterine gestation, most often a tubal pregnancy with its various manifestations, actually or potentially presents a clinical emergency.

Correct treatment at the right time is important in order to save the life of the mother and possibly that of the intrauterine fetus as well.

18 Central Street

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CLINICAL NOTE

A NEW METHOD OF GIVING
POTASSIUM IODIDE*

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POTASSIUM iodide has been used for many years in medicine as an alterative and in the treatment of syphilis. It has been employed in pills, capsules and saturated solution. All these are more or less irritating to the stomach. The

I have used these pills in a number of cases in which potassium iodide was indicated. All these patients responded as expected, showing that the iodide was absorbed. Tests were made to determine the rate of absorption and to determine whether the weight of the patient had any relation to the tolerance of the drug. The elapsed time between the ingestion of the enteric-coated pill and the appearance of iodine in the saliva was about one and a half hours, whereas the elapsed time between the ingestion of potassium iodide in capsule form or solution and the appearance of

TABLE I. Summary of Data.

PATIENT	AGE Yr.	TYPE OF SYPHILIS	SIGNS	DURATION OF TREATMENT	RESULT OF TREATMENT	REMARKS
P. S.	8	Congenital	Keratitis	1 wk.	Lesion subsiding	Lesion resistant to bismuth and arsenicals
C. M.	18	Congenital	Keratitis	3 wk.	Lesion healed	
E. H.	21	Secondary (recurrent malignant)		1 mo.	Lesions healed	Lesions resistant to bismuth, mercury and arsenicals
P. W.	21	Late	Gumma on right side of chin	1 mo.	Gumma healed	
A. C.	38	Late	Gumma on right thigh	1½ mo.	Gumma healed	
M. C.	58	Late	Multiple gummas	2 wk.	Gumma healed	
T. M.	60	Late	Multiple gummas	2 wk.	Gumma healed	
C. S.	60	Late	Gumma on right thigh, erythema of liver, with fluid in abdomen	4½ mo.	Gumma healed, fluid in abdomen absorbed	Metallic taste
I. S.	51	Late	Gumma on right lower leg	1 mo.	Gumma healed	
P. M.	47	Late	Gumma on chest	1½ mo.	Gumma healed	Fistulae on face
A. McL.	72	Late	Gumma on right foot	2 mo.	Gumma healed	
Q. J.	65	Late	Tubercles dorsalis	2 mo.	No change in symptoms	Metallic taste

saturated solution, in which form the drug is most commonly given, is considered to be the equivalent of 1 gr. per drop. The size of the drop, however, varies with that of the dropper and usually contains somewhat below this amount. It was therefore suggested that if an enteric-coated pill were used, both these objections could be eliminated.

Such a pill, containing 1 gm. (15 gr.) of potassium iodide,‡ was obtained. The enteric coating on these tablets does not dissolve until it comes in contact with the bile in the intestinal tract; it is insoluble in alkaline or acid solutions alone. This especially designed coating contains cetyl alcohol, gum mastic, balsam tolu, gelatin and sugar. Acetone and alcohol are used as solvents. Samples were tested in vivo and in vitro to determine their solubility.

iodine in the saliva was half an hour. Thus it can be seen that the absorption time of iodine was greater in the enteric-coated pill than in capsule form or solution. The tolerance to potassium iodide did not seem to depend so much on the weight of the patient as on his idiosyncrasy to potassium iodide.

The enteric-coated pill was given in 12 cases of syphilis in varying amounts (Table I). All the patients started with one tablet three times a day. Only 1 patient developed an iodide eruption. Two patients complained of a metallic taste. These reactions were considered to be due to idiosyncrasies. No patient complained of a stomach upset. There were 2 cases of congenital syphilis, 1 of which was a malignant type that did not respond to arsenical and bismuth therapy. One patient had recurrent malignant secondary syphilis, and 8 had late cases with gummas. All responded well to treatment. One was a case of tubercles dorsalis in which the dose was increased

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‡Obtained as Enclose through the courtesy of Brewer & Company, Inc., Worcester, Massachusetts.

to four tablets three times a day without any gastric symptoms that could be attributed to the potassium iodide.

SUMMARY

The use of potassium iodide in the form of an enteric-coated pill is described. Twelve cases so

treated responded well, and none complained of a gastric upset. Three patients evidenced idiosyncrasies to the drug. In view of the lack of gastric disturbances and the accuracy of dosage, further trial of this method of therapy is recommended.

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MEDICAL PROGRESS

UROLOGY*

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THE SULFONAMIDES

DURING the past year the knowledge of the great importance of the various sulfonamide drugs has become more crystallized. A noteworthy review and summary is that of Janeway,¹ with which every physician should be familiar. Written by an eminent authority on the treatment of infectious diseases, it is a comprehensive study based on his own large experience, as well as on the many articles in the literature bearing on this subject. The various forms of the sulfonamide drugs now in use are compared concerning action, dosage and toxic manifestations. There follows a discussion of their clinical use and what may be accomplished in the control of the various forms of bacterial infection. Being in itself a review, this article does not lend itself to summary.

In infections of the urinary tract, the sulfonamide drug that is today the one of choice is sulfadiazine. All types of urinary infection except those due to the enterococcus respond to its use. In most cases relatively small doses (2 to 4 gm. daily) are needed to attain the desired result, and thus good toleration and freedom from untoward manifestation are the rule. The outstanding drawback to sulfadiazine, however, is its low solubility and therefore slow excretion. Sulfathiazole is also well tolerated and is more soluble than sulfadiazine, but there is evidence that it is a fairly toxic drug, acting on the kidney parenchyma to depress renal function. Low solubility causes the precipitation of crystals in the renal tubules and ureters, with resultant hematuria or obstruction, reaching anuria in extreme cases. Indeed, there are reports of several deaths following such a sequence. It is imperative, therefore, that patients taking these drugs receive sufficient fluids to ensure a daily out-

put of urine of at least 2 liters. Blockage of the renal pelvis and ureters, should it occur, can generally be relieved by lavage through ureteral catheters, using a solution of bicarbonate of moderate strength. Both sulfathiazole and sulfadiazine are more soluble in an alkaline than in an acid urine, so that it is always wise to accompany their use by the administration of moderate amounts of sodium bicarbonate.

A more important manifestation of the toxicity of sulfonamide drugs is found in patients who have become sensitized by a previous administration of them. Such cases are not uncommon, and in view of the extensive use of the sulfonamides today, the recognition that such reactions may occur is certainly not sufficiently kept in mind by the physician in general practice. The following case is an example:

A 55-year-old man (PBBH S-71418) underwent the perineal removal of a benign prostatic enlargement. Because of a moderate amount of cystitis he received 2 gm. of sulfathiazole daily, beginning on the 3rd day after operation. The temperature, which had previously been normal, rose on the 8th day of this treatment to 101.5°F., when the drug was immediately discontinued, with a resultant return of the temperature to normal. The patient was discharged on the 14th day after operation, having good bladder function and a well-healed wound but still showing a mild cystitis, for the treatment of which he was referred to the Out-Door Department.

On the 12th day following discharge he was returned by ambulance to the hospital. The pulse was 120 and weak and thready, the respirations 20, and the temperature 103.2°F. The face was flushed and the eyes were bloodshot. The sensorium was much clouded, almost to coma. The blood pressure was 80/40 and the skin, especially of the back, shoulders and face, was a brilliant red. No adequate history was obtainable, but search of the Out-Door Department records showed that 4 days previously the patient had made a visit, at which time he had complained of dull pain in the right calf that made walking somewhat difficult. There was also a tender area on the inside of the calf. A diagnosis of mild thrombophlebitis of the leg was made. The patient was given a bandage and told to rest the leg at home. With this history in mind and the fear that the patient was suffer-

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp. Springfield, Illinois: Charles C. Thomas, 1942. \$5.00).

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ing from a blood stream infection, he was given immediately on entrance 1 gm of sulfathiazole together with parenteral fluid and the next morning, 8 hours later, he was given another gram of sulfathiazole. This was followed almost immediately by a severe chill lasting for 45 minutes, with a temperature of 106°F and an alarming fall in blood pressure (to 70/40). It became immediately evident that the patient's condition was due to drug sensitivity, and a detailed history obtained from his physician brought forth the fact that on the day before the patient's collapse the latter had prescribed sulfathiazole in an effort to clear up the infection in the urine. Two grams at once, followed by 0.5 gm doses every 2 hours, was prescribed. This medication was followed by vomiting on several occasions and cessation of urination, only 60 cc of urine being passed during the whole day.

Further physical examination showed the white cell count to be elevated to 16,600. The level of sulfathiazole in the serum was 4.1 mg per 100 cc., and the urine was concentrated and filled with sulfathiazole crystals. Treatment consisted of parenteral fluids in liberal amount and 1 unit (500 cc.) of plasma. After 2 days the blood pressure became stabilized at 120/80 and the urinary output rose to 350 cc. The blood urea nitrogen, however, was still high, reaching 51 mg per 100 cc. The patient was still acutely ill and disoriented. By the 5th day, however, the output of urine rose to 1800 cc, after which convalescence was continuous, although complicated by a slight pulmonary atelectasis and marked peripheral neuritis of the external peroneal nerve. The signs of acute nephritis slowly improved, and 5 weeks later the patient was discharged well.

It is evident that sensitivity to the sulfonamides has thus become a possibility that, because of their extensive use, must always be taken into consideration in acute febrile conditions associated with prostration. It is also true that such sensitivity may persist for at least as long as six months. In this regard the advice of Janeway cannot be too often repeated: "After the patient is cured, tell him which sulfonamide drug he has received; if he has had a reaction instruct him to inform any physician about it before taking sulfonamides again."

URINARY CALCULI

In order to facilitate the operative removal of small single or multiple calculi from the renal pelvis and its branches, Dees² suggests the formation of an intrapelvic clot that on removal contains any small concretions within itself. The clot is formed from a solution of human fibrinogen that is caused to coagulate by the simultaneous injection of a "clotting globulin" derived from rabbit plasma. These substances are injected simultaneously into the kidney pelvis after its capacity has been measured. The clot forms immediately, and at the end of five minutes has acquired sufficient tensile strength to make it possible to withdraw the mass as a cast of the pelvis and calyces through the usual pyelotomy incision.

It is pointed out that a suitable coagulating substance should have the following properties: it should be fluid so that it can be injected into the renal pelvis and fill it completely, it should coagulate uniformly and completely within a short period of time, but not until after a latent period sufficiently long to assure the complete filling of all calyces before coagulation, the strength of the coagulum should be sufficiently great within a short time after injection of the substance to permit its withdrawal intact and to deliver any calculi contained within it, the coagulum should be malleable and elastic enough to permit withdrawal of the mold of each calyx through its narrower infundibulum, and also to allow removal of the entire clot through a short incision in the renal pelvis, it should be noninjurious to the kidney, the coagulum should spontaneously dissolve or disintegrate so that if a fragment is accidentally left within the pelvis, it will not remain as a foreign body to cause further stone formation, and the properties of the coagulable substance should be unaffected by contact or mixture with small amounts of urine or blood. Dees finds that clotted fibrinogen, the properties and preparation of which he^{3,4} describes in two earlier papers, fulfills these requirements.

There is no doubt that the ability to produce such a coagulum within the pelvis and calyces offers the urologic surgeon a new method of much promise in the extraction of small fugitive concretions well known to be extremely difficult to locate or reach during the usual operative attack. Only too often irrigation, suction and stone forceps fail to rid the kidney pelvis and calyces of all such concretions, some of which must thus performe be left, to cause further difficulty. The entire innocuousness of the fibrinogen coagulum seems to have been well proved by its discoverer. A difficulty remains, however, for it is stated that 1 liter of human blood plasma yields only 40 to 50 cc of fibrinogen solution. It is to be hoped, therefore, that the present efforts to substitute bovine fibrinogen will meet with success.

Another distinct aid in the attack on urinary calculi consists in the *in vivo* solution of the calculus by exposing it to the solvent action of a mixture of citric acid combined with magnesium oxide and sodium carbonate in water.* After ex-

* Solution C is so termed by its makers has the following formulae:

Citric acid (monohydrate)	33.3 gm
Sodium carbonate (anhydrous)	4.4 gm
Magnesium oxide (anhydrous)	3.8 gm
Dissolved in water	q. s. ad 1000 cc

Solution C has a pH of 4.0. Another formula with a pH of 4.5 is given by the makers if the more acid solution causes irritation or hemorrhage. The formula of Solution M is as follows:

Citric acid (monohydrate)	33.35 gm
Sodium carbonate (anhydrous)	8.4 gm
Magnesium oxide (anhydrous)	3.84 gm
Dissolved in water	q. s. ad 1000 cc

perimental observations using many substances, Albright and his associates⁵⁻⁷ have found it possible by using such a solution to cause the dissolution of such calculi as are composed largely of calcium phosphate, without at the same time causing any significant irritation or injury to the mucosa of either the renal pelvis or urinary bladder. In clinical cases in which the stone can be bathed in such solution as nearly continuously as circumstances will permit, its removal has been successfully accomplished. Naturally if the stone is not accessible to the action of the solution, and especially if it is composed of a dense matrix of organic material, its entire dissolution will be imperfect. The easiest and most direct application of the solution to the stone is by a two-way tube introduced into the renal pelvis through a nephrostomy wound. But in several cases the desired result has also been obtained by an intermittent current of solution introduced through an indwelling ureteral catheter connected to an appropriate apparatus to produce filling followed by emptying by siphonage. When the stone lies in the bladder, a double catheter through the urethra forms easy access.

The observations reported in these papers raise hope that still further investigations of this interesting problem of stone dissolution will be forthcoming, such as the finding of Keyser⁸ that the addition of an enzyme—a 0.5 per cent solution of urease—to the citric acid solution causes an increase in the speed with which the stone is dissolved. At the moment, of course, patients bearing renal stones for whom attempts to dissolve the calculus are wise or justifiable are seen relatively infrequently. For the usual renal calculus, early operation together with the correction of the underlying cause of the stone formation, such as obstruction, infection or metabolic fault, is unquestionably the best course. But for those patients who have bilateral calculi, for example, and in whom each kidney already shows marked lowering of its functional ability, operation is often either very hazardous or even out of the question. For such patients, if their stone is of the phosphatic variety, which is usually the case, the use of Solution G or some future modification of it may be of the greatest benefit.

Further observations on the use and properties of Solution G have been made by Sauer and Neter⁹ at the New York State Institute for the Study of Malignant Diseases. Continuous-drip irrigation of the bladder was used for patients having incrustated ulcers of the bladder following the use of radium. Such late reactions after radium are not uncommon and are well known to be resistant to treatment. The lime salts of the urine are deposited on the surface of the ulcer in

the presence of an alkaline cystitis. "In almost all of the cases treated," Sauer and Neter state, "continuous-drip irrigation of the bladder with Solution G resulted in disappearance of the incrustations within one to three weeks, followed by healing of the ulceration. In 2 patients incrustated ulcers had persisted for more than seven years in spite of the normal treatment." These favorable results led the authors to make observations on the possible bactericidal properties of Solution G in addition to its solvent action. Four varieties of bacteria common in cystitis were used: *Escherichia coli*, *Proteus vulgaris*, *Proteus morganii* and *Streptococcus faecalis*. Each organism was found to have lost its viability within seventy-two hours after exposure to Solution G (pH 4.0), whereas they remained viable for two weeks in physiologic saline solution (pH 6.8). Further tests, however, made it probable that this bactericidal action was largely due to the acidity of the solution and that its particular composition does not increase its antimicrobial properties beyond those of a buffer solution of identical reaction.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., Editor*

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CASE 29511

PRESENTATION OF CASE

A seventy-seven year-old housewife was admitted to the hospital because of vomiting of one week's duration.

The patient was rather confused and could not give an accurate history. She had been in good health except that she had lost 50 pounds of weight during the preceding year in spite of a good appetite. Recently she had felt tired and rundown. Two or three weeks before admission she developed sudden abdominal pain. This was vaguely described as having started in the left lower quadrant or the right lower quadrant and became generalized. The pain was dull, severe and not colicky, and was accompanied by chills and fever. She was taken to a community hospital ten days before admission and given intravenous fluids for three days and then discharged against advice.

One week prior to entry she began to vomit constantly. No definite statement could be obtained regarding the character of the vomitus except that "after the first few days the material became progressively more fecal." The vomiting continued. She was unable to take anything by mouth. She was constipated and passed only small amounts of feces by rectum for the two days before entry; these were not "bloody." She had had no fever during the preceding week. She had always been somewhat constipated and took cathartics regularly. There was no history of jaundice or bloody, tarry or acholic stools. She had had no previous operations.

Physical examination showed a dehydrated woman retching and vomiting. She was not puny. The lungs were clear. The heart was slightly enlarged, with the left border of cardiac dullness 2 cm. to the left of the midclavicular line. The sounds were of poor quality and very irregular; occasional dropped beats were present. There was a loud apical systolic murmur and a harsh high pitched aortic systolic murmur. The abdo-

*D. J. Leve of Aben e

men was somewhat distended and tympanic. There was dullness in the flanks, but no shifting dullness or fluid wave. Moderate tenderness was elicited in the right upper and lower quadrants, and rebound tenderness and spasm in the right lower quadrant. The psoas and obturator signs were negative. Peristalsis was hypoactive but some tinkling was heard. The liver edge was one fingerbreadth below the costal margin and was nontender. No masses were palpated on abdominal, rectal or pelvic examination. There was pitting edema of the ankles.

The blood pressure was 144 systolic, 80 diastolic. The temperature was 98.6°F, the pulse 76, and the respirations 18.

Examination of the blood showed a red-cell count of 4,370,000 with 90 per cent hemoglobin. The white-cell count was 13,800 with 78 per cent neutrophils. A blood Hinton test was negative. The urine showed a specific gravity of 1.010, with a + test for albumin. The sediment contained innumerable white cells and occasional red cells. The nonprotein nitrogen was 120 mg per 100 cc and the protein 6.2 gm.

A roentgenogram of the abdomen showed a dilated transverse colon and some gas and considerable fecal matter in the cecum. Several dilated loops of small bowel, probably ileum, were seen.

A Miller-Abbott tube was passed, and 1750 cc of "brown fecal fluid" was aspirated with considerable relief. The aspirated material was guaiac negative. The patient was given daily intravenous fluids and occasional transfusions of whole blood. A barium enema on the second day showed ready passage of the opaque material to the cecum. There were many diverticula in the descending colon and sigmoid but no evidence of diverticulitis. The cecum was high, almost fixed, and extending downward from it was the appendix, which seemed to be filled with barium. No barium could be forced into the terminal ileum. Considerable difficulty was encountered in the passage of the Miller-Abbott tube, which seemed to remain in the stomach.

The patient continued to vomit material that was definitely fecal in character. She was unable to take anything by mouth. A roentgenogram of the abdomen on the third day showed retention of a large amount of barium in the colon. The dilated loops of small intestine appeared increased. An ileostomy was performed on the fourth day, with considerable relief. On the fifth day no dilated gas-filled loops of bowel could be seen by x-ray; those that were dilated appeared to be full of fluid. There was a large

increase in density overlying the right half of the pelvis. The nonprotein nitrogen was 86 mg., and the protein 5 gm. per 100 cc.; the chloride was 97.5 milliequiv. per liter.

The patient's condition improved considerably. There was copious drainage from the nasal tube and the ileostomy. Repeated attempts to pass the Miller-Abbott tube beyond the pylorus were unsuccessful. In the next four or five days the abdomen became much softer. Peristalsis was normal, and she passed some gas by rectum. There was no vomiting.

On the tenth hospital day an exploratory laparotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. CARROLL C. MILLER: This conference today seems to be concerned with obstruction in the region of the ileocecal valve.* Frequently mistakes have been made in the past in the diagnosis of gallstone ileus. It seemed during this discussion that the three cases might all be due to gallstone ileus. As we have seen, however, the gallbladder and biliary system have not been implicated in either of the two preceding cases. In the present case we have not only an acute episode to consider, but also a period of one year during which the patient lost 50 pounds in weight. Before the onset of the acute episode there had been a tired, run-down feeling. Then suddenly an acute episode occurred, which was obviously due to acute, low obstruction of the small intestine. As we go through the data that are available we find no definite evidence of an acute inflammatory process. The symptoms first noted were pain in the lower abdomen, distention, some tenderness and vomiting. Although these suggest peritonitis at the start, the subsequent course, the lack of marked elevation in the white-cell count and a polymorphonuclear shift, the absence of fever and other toxic signs and the presence of tenderness lead me to believe that the obstruction was mechanical rather than inflammatory.

If we consider the causes for mechanical obstruction of the low ileum, we think of adhesive bands, volvulus and intussusception. The x-ray films should be of considerable help. They substantiate the diagnosis of obstruction of the small intestine by showing dilated loops of small bowel with some degree of distention of the transverse colon. Quite correctly no series of the upper gastrointestinal tract was done, because at that time the exact site of the obstruction was uncertain.

May we see the x-ray films?

DR. GEORGE W. HOLMES: This first film shows a shadow on the right side interpreted as transverse colon filled with gas. Then the patient was given a barium enema to determine how much gas was in the colon and how much in the small bowel. You can see that there are loops of small bowel that are definitely distended and filled with gas. It also shows multiple diverticula along the distal colon, and the appendix is visible. I think that this probably rules out appendiceal abscess as a cause of the obstruction. What part of the small bowel this represents, I am not certain; but I should think probably the ileum and not the jejunum. We also have several other films taken within a day or two that confirm these findings. All these films show a residual in the colon following the enema. The patient was unable to evacuate the enema completely, and you can still see dilated loops. Then the Miller-Abbott tube was passed. On this film it was in the stomach, and later on it passed beyond the stomach but appears to have tied itself in a knot as the Miller-Abbott tube sometimes does. That would explain why the Miller-Abbott procedure was not effective.

DR. MILLER: In the last film there is mention of hazy dullness in the right half of the pelvis. Is there any discrete mass?

DR. HOLMES: That probably is an artefact. This film was taken with the tube off center, which changes the density. I do not believe that it is of any clinical importance. Evidently the man who did the examination was interested in this loop of bowel, because he took a number of spot films of it.

DR. MILLER: Is that loop a part of the sigmoid?

DR. HOLMES: Yes.

DR. MILLER: Showing the diverticula?

DR. HOLMES: Yes; so far as I can see from these films there is nothing more than that.

DR. MILLER: No evidence of inflammation or diverticulitis?

DR. HOLMES: There is some evidence of spasm. There may be slight diverticulitis, but I am sure that there is no tumor in that region.

DR. MILLER: The cecum is described as being high and fixed. Is it out of the right lower quadrant?

DR. HOLMES: Yes; but "high and fixed" by x-ray examination is not an absolute finding. It depends on the patient; if the patient has a soft abdomen, palpation is easy; if there is resistance, palpation is unsatisfactory. One may not be able to move the colon during the time of examination.

DR. MILLER: It would be convenient to postulate a tumor in the pelvis, which would account for

*Case records of the Massachusetts General Hospital (Cases 29501 and 29502). *New Eng. J. Med.* 229:948-953, 1943.

the loss of weight, owing to malignant degeneration and diffuse spread, and also for an obstruction of the small bowel. No tumor, however, was felt by either abdominal or pelvic examination, nor is one visible in any of these films. It would also be convenient to postulate a carcinoma of the bowel that had caused sufficient contraction around the loops of terminal ileum to produce the acute episode of obstruction and also to account for the debility in the year before the patient came into the hospital. If we do postulate carcinoma, however, I think it is unrelated to the obstruction. It must be present simply as an explanation of the loss of weight and the downhill course.

It seems to me that the best condition to explain such a picture in a patient of this type is one of adhesive bands or a volvulus of the terminal loop of ileum, or an intussusception that was not seen in the x-ray films. It is mentioned that no barium could be forced back through the ileocecal valve. This might have been due to a distorted ileocecal valve or to a definite obstruction other than the folds of the valve in that area. We have recently seen several patients, especially older women, who have come in with a similar story. Some had had previous operations; others had not. They were found to have either an atypical adhesive condition between the loops of small bowel or a twist of the loops to account for the obstruction.

One condition that I have not mentioned but which one should think of is an acute perforation of the terminal ileum or cecum by a foreign body, such as a fishbone. This might account for the suddenness of the onset of abdominal pain. It would also account for the localized inflammatory reaction, but it would not account, of course, for the loss of weight and malaise prior to admission to the hospital.

I am going to rest my diagnosis with an adhesive band or adhesions between the ileum and cecum causing acute intestinal obstruction, with or without associated carcinoma of the abdomen.

CLINICAL DIAGNOSIS

Obstruction of small intestine, with perforation due to foreign body.

DR. MILLER'S DIAGNOSES

Obstruction of small intestine due to adhesive band or adhesions.
Carcinoma of abdomen?

ANATOMICAL DIAGNOSIS

Gallstone ileus, with obstruction of small intestine.

PATHOLOGICAL DISCUSSION

DR. DONALD N. SWEENEY: This patient was as confusing to us as she was to Dr. Miller. We were unable to explain the loss of weight without making a diagnosis of carcinoma. We could not pass a Miller-Abbott tube and had to do a Witzel ileostomy for decompression of the small bowel. We operated ten days after the ileostomy, with a diagnosis of perforation of the small bowel due to a foreign body, as Dr. Miller suggested. During the exploratory laparotomy the small bowel involved in the ileostomy was inadvertently torn from the abdominal wall. In closing the rent, the lumen was constricted and an enteroenterostomy was done. During this procedure three small gallstones were picked from the lumen of the small bowel. In the right upper quadrant there was an inflammatory mass that involved the hepatic flexure of the colon, the gall bladder and a loop of jejunum. In the cecum there was a large mass, thought to represent a gallstone, that I was unable to push back into the small bowel, and which I was loath to remove by opening the cecum. During the patient's subsequent convalescence we were able to obtain four or five small gallstones from the stools, but we never recovered the large gallstone, which probably disintegrated.

The patient did extremely well and is coming back at a later date for a cholecystectomy.

DR. BENJAMIN CASTLEMAN: Here is a postoperative film. Is this shadow the stone in the cecum?

DR. SWEENEY: That is what Dr. Schulz of the X-ray Department thinks is stone and accumulated barium. It was about the size of a plum and was partially fixed in the ileocecal valve. I could push it into the cecum but could not get it back.

DR. MILLER: You do not know whether she has carcinoma of the gall bladder?

DR. SWEENEY: I do not. She may have carcinoma but I doubt it, because she did so well postoperatively and has regained 10 of the 50 pound weight loss in the four weeks since she was operated on.

DR. MILLER: The fact that she had tenderness in the right upper quadrant should have made me think of an acute process going on there. The tenderness over the distended colon or small bowel was also confusing.

DR. CASTLEMAN: Do you think that that is a gallstone in the postoperative film, Dr. Holmes?

DR. HOLMES: Yes; it obviously was not in the cecum in the previous films.

DR. SWEENEY: There was some talk about air in the biliary tract. Now that we know the whole story we think that we can see air in the bile ducts

DR. CASTLEMAN: Do you agree with that, Dr. Holmes?

DR. HOLMES: I did not notice it in the films. There are shadows there that might possibly be due to that. To demonstrate air in the biliary tract one ought to take a film with the patient sitting up.

CASE 29512

PRESENTATION OF CASE

A forty-seven-year-old taxidriver was admitted to the hospital because of cough and weakness of six months' duration.

The patient was a chronic alcoholic, as well as a Seconal and paraldehyde addict. He had consumed large quantities of whisky since the age of twenty and had had repeated attacks of hallucinations and tremor, for which he had been hospitalized. About two years before entry he changed from whisky to ale, but he imbibed large amounts of the latter. There was a steady deterioration of memory, so that it was quite difficult to obtain a history and he was unable to give much information. His general condition had apparently been good until about two years before admission, when he noted episodes of fever as high as 102°F. associated with weakness and a cough productive of phlegm. The episodes of fever presumably continued until eight months before admission, when he started to feel tired and worn out, with progressively increasing weight loss and fatigue. There was some exertional dyspnea for the six weeks before entry, but no orthopnea, paroxysmal nocturnal dyspnea, hemoptysis, ankle edema or swelling of the abdomen. Three or four days before admission he developed a diarrhea consisting of eight or ten liquid, light-brown stools daily. There was no nausea, vomiting or bloody or tarry stools. During this period he had eaten little, subsisting on rather large quantities of ale. No other statement was made about his dietary habits.

Physical examination showed a well-developed man with evidence of recent weight loss. The skin was hot and moist. The mucous membranes were pale. The pupils were irregular but equal and reacted sluggishly to light. The tongue was dry, the teeth dirty and carious, and the gums pyorrheic. The lungs were resonant throughout, but there were coarse rhonchi, squeals and groans, with a prolonged expiratory phase, throughout both fields. Patchy areas of diminished breath sounds were present, and moist rales were heard at both bases. The diaphragmatic excursion was poor on the right side. The heart was normal. The abdomen was distended, with the liver edge

palpable three fingerbreadths below the right costal margin. The spleen was felt five fingerbreadths below the left costal margin. The flanks were full, but no demonstrable fluid wave or shifting dullness was present. There was a coarse tremor of the outstretched hands, and minimal pitting edema of both ankles. Rectal examination showed palpable thrombosed external and internal hemorrhoids with one large external tab.

The blood pressure was 110 systolic, 65 diastolic. The temperature was 102°F., the pulse 120 and the respirations 30.

Examination of the blood showed a red-cell count of 3,750,000 with 9 gm. of hemoglobin. The white-cell count was 1500, with 55 per cent neutrophils, 34 per cent lymphocytes and 11 per cent monocytes. The platelets were diminished, and there was moderate anisocytosis and poikilocytosis. The urine showed a specific gravity of 1.015; the sediment showed 8 to 15 white cells and occasional red cells and coarse granular casts per high-power field. The sputum contained innumerable polymorphonuclears and moderate numbers of diplococci; it was culturally negative for beta-hemolytic streptococci and pneumococci. The stools were yellow, liquid and guaiac negative. No amebae were seen after "diligent search," and a culture was negative for pathogenic bacteria. The non-protein nitrogen was 22 mg. per 100 cc., and the chloride 95.5 milliequiv. per liter. The van den Bergh was 0.65 mg. direct, and 0.85 mg. indirect. The serum protein was 6 gm. per 100 cc. The cephalin flocculation test was ++ in twenty-four hours and ++++ in forty-eight hours.

An x-ray film of the chest showed several linear areas of increased density, probably atelectasis, in the right lung, but no areas of infiltration were apparent. The heart and aortic shadows were not unusual. Films of the abdomen showed the liver and the spleen to be enlarged. The entire abdomen was moderately and homogeneously clouded, probably because of ascites.

In the first four days the temperature showed one rise to 104 and one to 103, but fell gradually to 99.4°F. During that time the patient received three intravenous infusions of 1500 cc. of dextrose in water. He was given a high-calorie and high-vitamin diet. On the fifth day he had a mild attack of asthma lasting for about half an hour, which was relieved by ephedrine. His general condition seemed to improve, and by that time further information was obtained from one of the hospitals where he had been. It was stated that for the previous eight or ten months the patient had been having attacks of fever up to 103 or 104°F. that lasted several days, with afebrile in-

tervals of three or four weeks. He had been studied for malaria, but no malarial parasites had been found and no quinine had been given.

On the sixth, seventh and eighth hospital days the patient's temperature varied daily between 99 and 105°F. He had two chills. Three blood cultures were negative. A Widal test was negative. Additional information revealed that for the eight or ten months prior to admission, he had been taking sulfathiazole in doses of 1 or 2 tablets every hour for about three or four hours every time he had an episode of fever. In the past six weeks he had been receiving sulfadiazine intravenously, which was given by his physician each time he was called in for high fever.

An x-ray film of the chest on the thirteenth hospital day showed numerous fine linear areas of increased density in the right midchest, with some suggestion of honeycombing. There were no gross areas of consolidation or atelectasis, and no definite evidence of fluid. The white-cell count was 1600.

The patient's condition became steadily weaker, with a progressive rise of temperature to 106°F., and he died on the fifteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. REED HARWOOD: In summary we have a chronic alcoholic with a deficient food and vitamin intake who developed cirrhosis of the liver and had chronic bronchitis and asthma. He also had a chronic infection characterized by severe exacerbations with fever and chills, and died with marked leukopenia.

I should like to look at the x-ray films at this point.

DR. GEORGE W. HOLMES: The first films were taken in July, and the second set in August. There is nothing striking or characteristic about either set of films. I am interested to know whether his heart was normal. It looks normal, although the left border does appear a little prominent. The diaphragm is in the usual position. In the second set of films, something that looks like dilated bronchi appears that was not present in the previous films; that is of considerable importance. If we did not have the previous films we might interpret this as being of no importance but since it appeared in a month I think it must mean something.

DR. HARWOOD: Do you think there is sufficient disease in the lungs to account for death?

DR. HOLMES: I do not believe this condition in the lungs had anything to do with his death.

In the film of the abdomen, you will notice that the film is rather thin, although the exposure was normal. Evidently there was some difficulty

in getting through the abdomen, which suggests the presence of fluid. Then we have the shadow of the liver and the shadow of the spleen, both of which are large. I think that I can say from the x-ray examination that the patient had an enlarged spleen and an enlarged liver; the shadow of the liver does not suggest the irregularity that may be present with a tumor.

DR. HARWOOD: As I went over the record, I came to the conclusion that this patient had a pulmonary infection, which was responsible for his final illness, but on rereading the x-ray report I wondered if enough had occurred in the chest to account for his death. I believed that Dr. Holmes would give the report that he has given, that is, that the lungs were not so striking as I had first thought. That leaves me "out on a limb" for a diagnosis, and I am going to beg your indulgence while I flounder around for a while and discuss the possible causes of fever.

It still is possible that the patient had an infection with its chief focus in the lung, but I am beginning to think that that is unlikely. Some of the conditions that I had thought of are pulmonary tuberculosis, carcinoma of the bronchus and bronchiectasis or other specific infections of the lungs, such as moniliasis, but there was no hemoptysis or organisms in the sputum. Bronchiectasis is unlikely because of the absence of foul sputum and clubbed fingers. Another relatively rare condition is chronic Friedländer's infection of the lungs, which occurs frequently in alcoholics, with a marked tendency to recur with severe exacerbations, responds somewhat to sulfadiazine, and can produce small cavities and bronchial dilatation. I am inclined to think now, however, that we shall have to consider something elsewhere in the body as the cause of this patient's death.

I interpret the leukopenia as evidence of bone-marrow depression, due to a combination of liver cirrhosis and acute infection. The possibility that the patient had a primary blood dyscrasia, such as aleukemic leukemia, seems highly unlikely in view of the normal smear. He has a moderate secondary anemia, which goes with any chronic sepsis, as well as with cirrhosis of the liver. The question of amebiasis was raised, but the story is not at all characteristic of amebic infection. The diarrhea developed late in the disease, no parasites were found, and the stools were not bloody. He might have had previous bouts of diarrhea that we do not know about. An amebic abscess of the liver is a possibility.

The question of malaria was raised. Again, the story does not seem good for malaria. Absence of parasites in the smear are the strongest bit of

evidence against such a diagnosis. He might at one time have developed central-nervous-system syphilis, for which he had been given malarial treatment. Even if this were so, at this late stage one would expect to find malarial parasites in the blood if his chills were due to this cause.

The question of a toxic reaction to sulfonamides comes up. I interpret this somewhat as follows.

dence to suggest it. The possibility of subacute bacterial endocarditis ought to be considered in any case of fever of unknown origin with leukopenia and a fatal termination. The patient, however, had no heart murmurs, and no physical signs suggesting embolic phenomena.

I must conclude, if one can call it a conclusion, that he died of some infection superimposed on

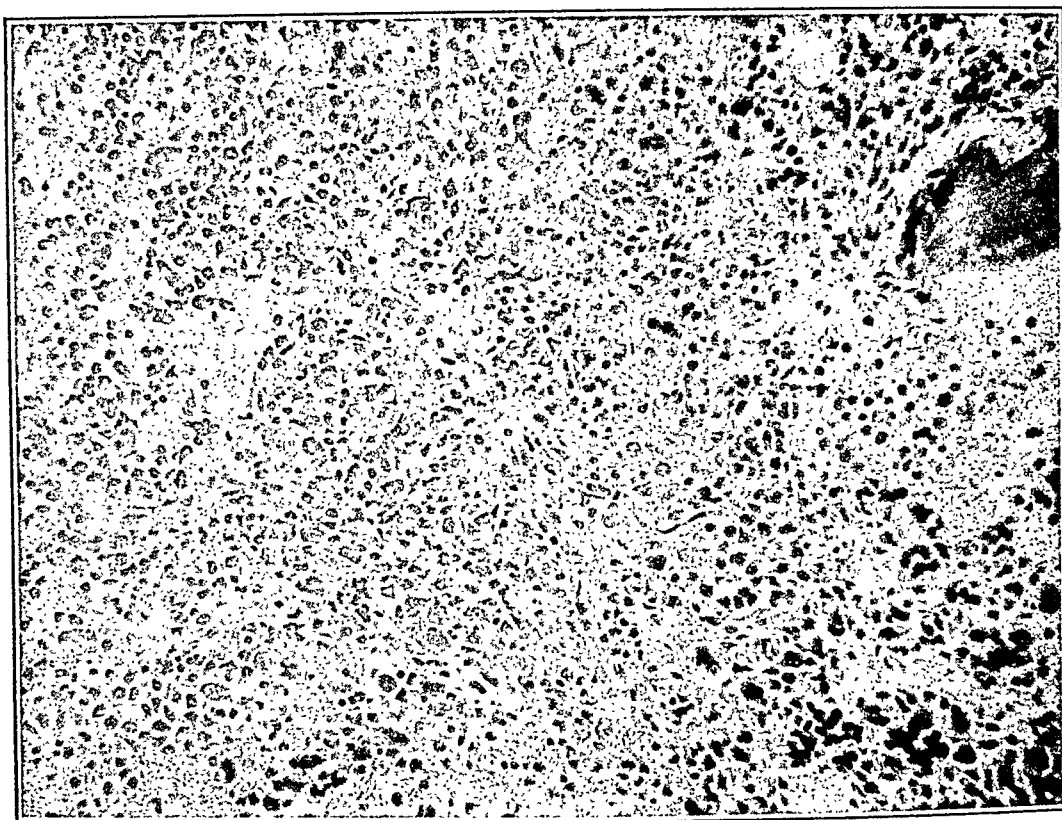


FIGURE 1. *Photograph of Section of Bone Marrow.*

The doctors who gave him sulfathiazole and sulfadiazine must have noted some response to the drug to justify their using it. In my original summing up of the case, I thought the patient had some chronic infection of the lung, with exacerbations that were relieved by sulfathiazole therapy, but now I am not so sure that the administration of sulfonamides had any bearing on the case or on the bacteriology. I do not believe it caused the leukopenia. It is more apt to cause a granulocytopenia, and this man had enough neutrophils in the differential count to make me think he did not have granulocytopenia.

He may have had some other type of infection to cause his chills. I cannot rule it out. He may have had peritoneal infection, such as tuberculous peritonitis. I do not see how I can exclude it. Fever and chills of this severity, however, are rather unusual in tuberculous peritonitis.

Did he have carcinoma somewhere in the liver or elsewhere in the abdomen? There is no evi-

cirrhosis of the liver. What it was, I really do not know.

DR. AUSTIN BRUES: Dr. Harwood will be glad to know that our clinical impression was also indefinite. One suggestion brought up by the service was that, in view of the leukopenia, anemia and thrombocytopenia, he might have disease invading the bone marrow, and the question of lymphoma was raised.

DR. JOSEPH AUB: What about the possibility of pylephlebitis?

DR. BENJAMIN CASTLEMAN: He did not have jaundice.

CLINICAL DIAGNOSES

Chronic alcoholism, with deterioration.
Alcoholic cirrhosis.
Bronchiectasis.

DR. HARWOOD'S DIAGNOSES

Chronic sepsis.
Alcoholic cirrhosis of liver.

ANATOMICAL DIAGNOSES

Bone-marrow hyperplasia of red-cell series, marked.

Hematopoiesis, marked: spleen, liver and lymph nodes.

Chronic benzol intoxication?

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy on this man showed an extremely large liver, which weighed over 2500 gm. It was smooth, purplish brown and rather firm and showed no evidence of cirrhosis. The spleen also was large, weighing 1010 gm., which is about five to six times the normal weight. This also was smooth and on section rather "meaty." From the gross examination we could definitely rule out cirrhosis of the liver as the primary cause of the large liver, and also the acute alcoholic liver, which is yellow and fatty. At the time of autopsy we were unable to make any definite diagnosis except enlarged liver and spleen; because of the marked anemia, the leukopenia and the meaty spleen, we thought the best diagnosis was some form of leukemia.

This man did have a bone-marrow biopsy before death, and this is the microscopical picture (Fig. 1). It shows extreme hyperplasia of the marrow. Normally this marrow should be made up predominantly of fat cells, but they are practically all replaced by marked hyperplasia of the marrow cells. Most of these cells are large stem cells and megakaryoblasts; there are a fair number of normoblasts and a few megakaryocytes, but the myeloid elements are scarce. In some places there is fibrosis of the marrow. The bone marrow from the material obtained at autopsy was the same. Sections of the spleen, liver and lymph nodes show these same cells of the red-cell series and also many multinucleated cells. The appearance is sim-

ilar to that reported a few years ago from this laboratory by Drs. Mallory, Gall and Brickley* in cases of chronic benzol poisoning. In some of their cases there were multinucleated cells that resembled the Sternberg-Reed cells seen in Hodgkin's disease, and a number of these cases have in the past been incorrectly called Hodgkin's disease. This man was a taxicab driver and may well have been exposed to benzene (benzol), although clinically they were unable to elicit any history of exposure.

I do not believe the sulfonamides had anything to do with his condition because there were plenty of polymorphonuclear cells in the bone marrow and in the peripheral blood.

DR. HOLMES: Did he have anything in the lungs?

DR. CASTLEMAN: The lungs showed bronchitis and mild bronchiectasis. Some of the bronchi, especially those in the right lower lobe, were moderately dilated.

DR. HOLMES: Were there any changes in the heart?

DR. CASTLEMAN: No.

DR. AUB: May I object very strenuously to a diagnosis of benzol poisoning? I think you have a right to say the patient died with a blood dyscrasia but have no right to say benzol poisoning unless you know he was exposed to benzol.

DR. CASTLEMAN: I agree. The pathologic picture is similar, and that is as far as one can go. Often, however, a history of benzol exposure is difficult to trace.

DR. BRUES: It is illuminating to note that this presumably toxic condition mimicked Hodgkin's disease in the type of fever as well as in the pathological findings.

*Mallory, T. B., Gall, E. A., and Brickley, W. J. Chronic exposure to benzene (benzol). III. The pathologic results. *J. Indust. Hyg. & Toxicol.* 21: 321-393, 1939.

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VARIOUS FREEDOMS

THE enunciation of the Four Freedoms established a goal to thrill the hearts of free men and bring hope to the subject masses of less fortunate countries than our own. The thought of freedom has always been an inspiration to mankind—a torch that has lighted the steps of many millions of feet, regardless of where their path ended. Sought after by the majority of the world's inhabitants, freedom remains an elusive abstraction,—a will-o'-the-wisp,—the concept of which may assume as many forms as there are minds to entertain it.

It was a canny idea to enumerate certain free-

doms in the plural number for there is not and cannot be such a thing as pure, unmodified freedom; personal freedom must always be qualified by the right to freedom of others and must always be restricted by the natural boundaries that are set to our thoughts and to our enterprises. It is a bold stroke to promise even certain freedoms to others. It is something else to guarantee the survival of these freedoms, or even their temporary enjoyment.

In those shadowed sections of the globe where freedom has been totally eclipsed, any kind of an emancipation is going to seem, at first, a sufficient goal. Later on, when the eye has become accustomed to the initial light, the qualifications and restrictions will be seen, and it will be noted that liberty can appear in various shades and colors.

The people of the United States, having set out to assure at least four freedoms (including the freedom from fear, from which no one is free) to the stricken people of the world, might do well, without pausing in this task, to see how freedom is working out in our own country. It becomes increasingly apparent that we must learn, if we wish to consider ourselves as the exponents of democracy before the world, that true democracy can exist only where its benefits are considered as a sacred trust and are spread equally over all the people without regard to race, creed or color. In this we have failed in that we have allowed ourselves to develop and nourish feelings of class hatred, of race and color discrimination and of religious prejudice. Democracy, tough as it may be when faced with dangers from without, is highly susceptible to dangers from within, and we can flourish only when its freedoms are uniformly distributed.

It will require a consistent, conscious effort of all thoughtful people to overcome the prejudices on which they have been raised, and to measure each man by his own worth rather than by the color of his skin, the cast of his countenance, or the building in which he worships, but it is the task to which we must set ourselves, and it must

be reciprocal. These problems that we have allowed to develop will continue to rise and accuse us, and we are going to have our hands full with them.

Bureaucracy will try to keep its hand on the helm and increase its powers, as it has always done, and, since bureaucracy is essentially sadistic, it will constitute an ever-present threat to democracy and those freedoms that are still left after the fight for freedom is finished. Here, too, lies our own greatest danger, in the federalization of medical practice. If this comes in, individual enterprise goes out, and another freedom with it.

THE PROBLEMS OF LOCAL HEALTH OFFICERS

EVER since the General Court of 1849 authorized the appointment of a commission of three members to "prepare and report . . . a plan for a sanitary survey of the State"—an authorization that brought about the famous Lemuel Shattuck report—there have always been available in Massachusetts a number of codes, suggestions and recommendations for workers in the fields of public health. These various plans have generally outrun our actual performances, which makes us appear to be constantly lagging behind what we might or ought to be accomplishing.

Under the leadership of another Shattuck in 1943, the Massachusetts Central Health Council has recently adopted recommendations concerning the problems of local health officers that represent the combined thinking of an enlarged and representative committee of that organization. It is the opinion of this committee, "That all cities of 50,000 population or over be required, and that all communities over 25,000 be urged, to employ a full-time health officer." The committee's report then goes on to suggest ways in which a community whose financial status does not permit it to meet these standards may combine with other communities to secure effective health services. Towns and unions of towns may organize in this

way under Chapter 111, Section 27A, in the Commonwealth of Massachusetts, and may thus secure for themselves a health-department organization that possesses many of the advantages of a large city department.

That so many of the small communities have not organized their health activities on this basis again suggests that they may be lagging behind their opportunities. Some of them doubtless are, but others are faced with obstacles of a local nature that must be overcome before they can improve their health services. The resistance that can be offered by a politically entrenched individual or group may be formidable. In the United States such resistances must be overcome locally, and by the time they have been overcome at one point they may have reappeared at another. Town meetings are notoriously suspicious of blueprints. Improvements in public-health practice must continue to evolve slowly, as they have in the past, but it is nevertheless helpful to keep plans for the future in mind and ready to activate when the propitious moment arrives. It is in this way that such organizations as the Massachusetts Central Health Council are building for the future.

MEDICAL EPONYM

PANCOAST SYNDROME

In an article entitled "Importance of Careful Roentgen-Ray Investigations of Apical Chest Tumors," by Henry K. Pancoast (b. 1875) in the *Journal of the American Medical Association* (83: 1407-1411, 1924), the following is described:

There is an unusual but apparently infrequent type of intrathoracic growth occurring in the apical region, yet found with sufficient frequency in my experience to warrant a collective report of the cases encountered. . . .

An infiltrating growth, either endothelioma of the pleura or sarcoma, probably of bony origin, may occur in the apex of the thoracic cavity and produce a symptom complex of pain in the upper extremity and cervical sympathetic paralysis closely simulating that of many other conditions, such as spinal cord or meningeal tumors, neck tumors, cervical rib and vertebral neoplasms.

Dr. Pancoast amplifies this description and re-names the tumor in an article "Superior Pulmonary Sulcus Tumor: Tumor characterized by

pain, Horner's syndrome, destruction of bone and atrophy of hand muscles," which appeared in the same journal (99: 1391-1396, 1932).

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

FOSTER—CHARLES C. FOSTER, M.D., of Cambridge, died December 2. He was in his eighty-sixth year.

Dr. Foster received his degree from Harvard Medical School in 1883. He was a member of the Massachusetts Medical Society and the American Medical Association.

GEARY—CORNELIUS E. GEARY, M.D., of Fitchburg, died December 6. He was in his sixty-fourth year.

Dr. Geary received his degree from Harvard Medical School in 1907. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, his mother, a daughter and two sons survive.

HARTWELL—HARRY F. HARTWELL, M.D., formerly of Newton, died December 7. He was in his seventy-first year.

Dr. Hartwell received his degree from Harvard Medical School in 1898. After a surgical internship at the Massachusetts General Hospital, he began the practice of surgery in Boston, and in 1904 was appointed assistant in orthopedic surgery at the Massachusetts General Hospital. In 1911, he became assistant surgical pathologist, and in 1916 gave up private practice to become surgical pathologist at the Massachusetts General Hospital, as well as a member of the Department of Pathology at Harvard Medical School. He served with the First Harvard Unit of the British Medical Corps during the early years of World War I, later enlisting as a surgeon in the United States Naval Reserve. He was a member of the Massachusetts Medical Society and the American Medical Association.

Two sons survive.

KENNEDY—EDWARD A. KENNEDY, M.D., of Pittsfield, died December 14. He was in his sixty-fourth year.

Dr. Kennedy received his degree from the University of Vermont College of Medicine in 1905. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow and three daughters survive.

TILTON—JOSIAH O. TILTON, M.D., of Lexington, died December 2. He was in his ninety-first year.

Dr. Tilton received his degree from the New York University Medical College in 1882. He was a member of the Massachusetts Medical Society and the American Medical Association.

WOOD—BENJAMIN E. WOOD, M.D., of Canton, died December 26. He was in his sixty-fourth year.

Dr. Wood received his degree from Harvard Medical School in 1906. He served his internship in the Children's Hospital, following which he was a surgeon on the staff of the Lawrence General Hospital, the Carney Hospital, and the Boston Dispensary. He was a member

of the Massachusetts Medical Society, the American Medical Association and the Orthopedic Club of Boston. His widow, two sons and a sister survive.

MISCELLANY

LYMPHOGRANULOMA VENEREUM

Noteworthy contributions to the detection and differential diagnosis of lymphogranuloma venereum are those of Rake, McKee and Shaffer, who have cultivated the agent in the yolk sac of the chick embryo and obtained concentrated suspensions of elementary bodies. In this manner a highly purified and specific skin-testing antigen, known as Lygranum S. T., has been prepared that is rapidly supplanting antigens prepared from either human pus or mouse brain. These workers alone, and in collaboration with Dr. A. W. Grace, have used the yolk-sac antigen for the complement-fixation testing of serum from suspected infected patients. The specificity and sensitivity of this antigen (Lygranum C. F.) provides an additional means of detecting early cases of lymphogranuloma venereum.

In the course of investigations involving these tests, there accumulated at the Squibb Institute for Medical Research a considerable mass of information concerning the properties of the causative agent and the epidemiology and clinical course of the disease. To facilitate the work of investigators and teachers in this field, and perhaps to encourage the interest of potential investigators, practicing physicians and health officers, it was decided to compile and publish the information at hand. The result is a 32-page monograph entitled *Lymphogranuloma Venereum*. The value of the book is enhanced by maps, charts and numerous illustrations in color.

The monograph is available gratis to physicians and to public-health officials, and should be a valuable addition to medical libraries. Those who request copies from E. R. Squibb and Sons, 745 Fifth Avenue, New York 22, New York, should enclose their professional card or use their professional letterhead.

ANNUAL PRIZE SUBSCRIPTION

The annual prize subscription offered by the *New England Journal of Medicine* for the best undergraduate contribution to the *Tufts Medical Journal* has been awarded to Roy Crosby, '44, for his paper "Medical Review: Recent advances in the diagnosis and treatment of prostatic carcinoma," which appeared in the October, 1943, issue. The paper "Medical Review: Gonorrhea in the adult female," by Alfred Agrin, '44, received honorable mention; it appeared in the August, 1943, issue. The basis of the award has been changed, allowing a two-year and one-year subscription to the *Journal*, respectively.

NOTES

On December 1, Dr. Harvey Spencer resigned as acting director of the Habit Clinic for Child Guidance and psychiatrist at the Judge Baker Guidance Center of Boston to become a member of the full-time psychiatric staff of the Austen Fox Riggs Foundation, Stockbridge.

At a recent meeting of the Board of Directors of the Washingtonian Hospital, Dr. Hilbert F. Day was elected

president, and Dr Norbert A. Wilhelm vice president, of the board

CORRESPONDENCE

PHYSICIANS AND BLOOD BANKS

To the Editor: The September 16, 1943, issue of the *Journal* contained an editorial entitled "Blood Plasma," wherein the lack of donors and the lack of physician co-operation were commented on in regard to blood banks in various hospitals. In contradistinction to this apathy noted, we, in Worcester, are enjoying an excellent spirit of co-operation with all physicians and donors. Since there is such a marked difference, it might be helpful to examine and discuss the reasons for it.

The Worcester Blood Bank (officially named the Worcester District Community Center for Aiding Transfusions, Incorporated) is sponsored by the Worcester District Medical Society and is aided by funds granted by the Worcester Chapter of the American Red Cross, the Worcester War Relief Fund, and the Community Chest of Worcester. The blood bank began to operate on October 12, 1942. It supplies whole blood and blood plasma to any hospital and to any physician in the entire Worcester district on request and without profit. In addition, it has already stored more than 2000 units of frozen blood plasma for any major catastrophe.

The blood bank is not located in a hospital but rather in a building of central location and actually a former private home. Here, blood is collected and processed and stored. Frozen blood plasma is also distributed to storage depots throughout the district, these depots being hospitals and establishments having the proper refrigerating facilities.

In this way it has been found possible to meet adequately the daily needs of the entire district at any time and at reasonable cost. This arrangement thus truly serves the community, a fact which the public has been quick to recognize and which is, without a doubt, a reason for the popular donor and physician support that has characterized the operation of the Worcester blood bank since its inception. In these times when people are increasingly alive to social betterment and improved medical and hospital care, the above fact might even be claimed to be a most potent one.

It is wondered if the chief defect in the administration of most blood banks is not that they are operated by hospitals. In the first place the cost of establishing and running a blood bank is such that only a large or financially well-endowed hospital can afford to have one. Here it must be pointed out that no matter how humanitarian the motives, in the minds of the people that blood bank serves a special group, that is, the patients in that institution and the staff of that institution. Consequently the blood bank tends to be supported mostly by those people who have special interest in that hospital. Since a blood bank for successful operation depends on a constant and satisfactory flow of donors, it is easy to envision that a hospital-operated blood bank will often be in difficulty in this respect. Especially is this true where the sole service running the blood bank does not enjoy the sole service to the community in which it is situated. Furthermore—and again no matter how humanitarian its motives in establishing the blood bank—a hospital cannot set up a bank of a size to meet much more than its own needs, because it is not in that business and because the cost is

prohibitive. Finally, it should also be remembered that the physicians most interested in a hospital-operated blood bank, namely, the staff, comprise but a small percentage of the practicing physicians in that community and consequently the staff's influence on prospective donors is correspondingly small. All these factors then, from within as well as from without, make one raise the question whether such an arrangement can ever call forth a great degree of popular support.

On the other hand, a blood bank managed as the one here in Worcester has intrinsically more with which to appeal to the public and elicit a satisfactory donor response. It is devoted to the needs of all physicians and not merely to a small and select group. It is large enough to meet the needs of all, whether the necessity for whole blood or blood plasma arises in the home, in the street, in the factory or in the hospital. Lastly, it does benefit all. In a little more than a year of operation, the services rendered by the Worcester blood bank to all institutions and all physicians in the district have multiplied almost ten fold. In terms of lives saved and the quicker recoveries effected, this is not an inconsiderable and unenviable record.

In conclusion may I say that the fine enthusiasm and active co-operation of physicians and public alike have more than compensated for the work and planning that went into the project, and have justified the hopes of the members of the Worcester District Medical Society. It has demonstrated what can be accomplished by the voluntary and co-operative effort of physicians in broadening the base of medical service without incorporating the inherent defects of governmental action.

WILLIAM FREEMAN, MD

281 Lincoln Street
Worcester, Massachusetts

TRANSFUSIONS WITH RED CELL SUSPENSIONS

To the Editor: Although whole-blood transfusions have been used as a therapeutic measure more and more in recent years, interest in plasma transfusions now seems to be paramount. Theories concerning the effect of plasma in shock and burns have focused attention on plasma in such a way that blood banks have been developed and the processing of plasma is a daily routine procedure. The latter, of course, leaves a portion of donors' blood—the red cells—that is usually discarded. Several investigators have demonstrated that it is practical to use these red cells, provided they are not over eight days old, for the treatment of anemic patients, these men, however, all deal with large blood banks having the advantage of a quick turnover. This letter deals with the problems of a bank in a small hospital, in which whole-blood transfusions average ten per month, with a much more frequent use of plasma.

In dealing with a bank in a small community, it is difficult to procure donors to build up an adequate plasma reserve, unless the hospital happens to be the official station for Red Cross donors. Furthermore, it is obvious that little whole blood can be kept on hand. Pooling is done within three or four days, and when occasion arises for using whole blood, the attending physician usually finds none available and is required to call for donors. This is time consuming, and the usefulness of the blood bank is thus diminished.

floor and roof of the subacromial bursa, and consequent loss of the gliding function normally present there. Instead, scapulothoracic motion results,

this basic etiology has been responsible for much ineffectual treatment.

CLINICAL FINDINGS

A patient with chronic adhesive subacromial bursitis seeks medical advice for persistent pain in the shoulder, oftentimes extending up into the neck as well as down the arm into the hand; marked loss of shoulder-joint function, or both. Not infrequently the latter complaint is the only cause of disability. Pain may have been of long duration, but by the time the patient is seen in consultation the pain has often largely disappeared, leaving the shoulder with marked limitation of motion.

Depending on the duration of symptoms, the patient reveals atrophy of the musculature of the shoulder region, to a greater or less degree. It is sometimes pronounced. Furthermore, some patients also complain of pronounced loss of finger joint function (Fig. 4). The hand is swollen and is similar in appearance to that seen in atrophic arthritis. In all our patients with this complication, the finger joints of the affected extremity were the only articulations that exhibited these changes, and therefore there was no question of a generalized rheumatoid arthritis.

The particular shoulder motion lost is that of external rotation and lateral abduction. Anteroposterior motion is usually of almost normal range. The patient can rotate the arm internally so that the forearm lies across the front of the body, but he can rarely pass the hand behind the low back or even place the hand on the hip.

Although local points of tenderness over the shoulder are present, they are less acute and less well localized than those exhibited by patients suffering from an acute subacromial bursitis with calcification. In patients with calcification and adhesive bursitis, local tenderness is more accurately defined. When requested to abduct the arm, the patient performs this motion by a combination of scapulothoracic motion and lifting the entire shoulder high on the affected side while the opposite shoulder is depressed (Fig. 5). On passive motion, assuming that the patient can be persuaded to relax, the humerus is abducted laterally from the side of the body, on the average 15 to 20°, at which point the scapula starts to move toward the axilla. If the scapula is held firmly, further passive or active lateral abduction of the arm is not possible.

The roentgenograms of the shoulder of a patient with chronic adhesive subacromial bursitis consistently reveal generalized atrophy of the bones of the shoulder girdle (Fig. 6), and in some cases this degree of decalcification of bone is pro-

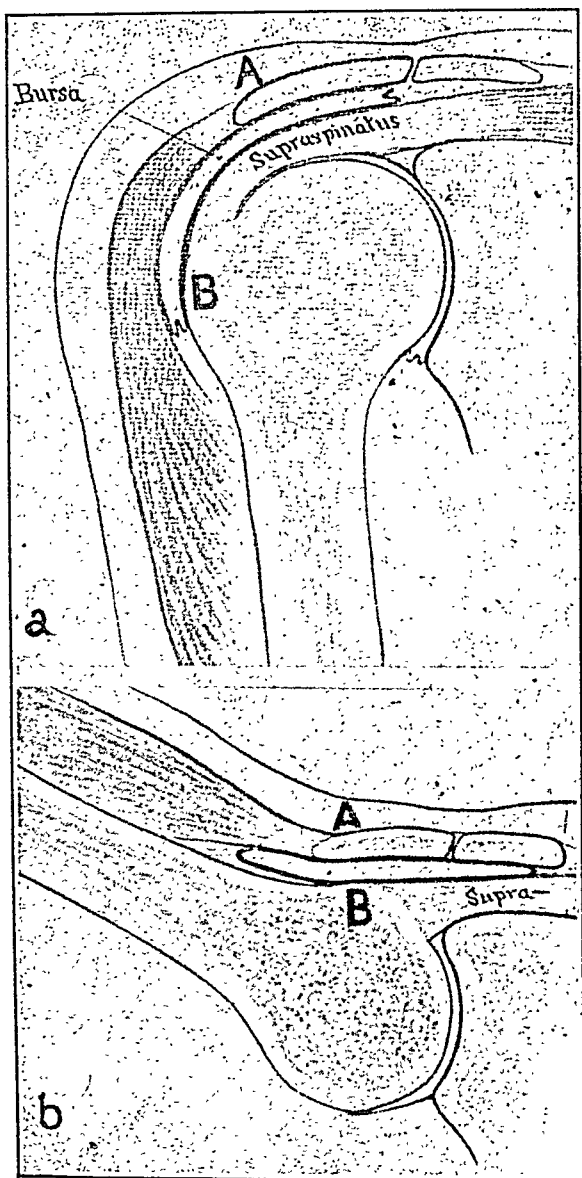


FIGURE 1. Diagrammatic Representation of a Coronal Section of the Shoulder Joint.

This shows the relation of the subacromial bursa to the adjacent bone and muscle structures (reproduced from Codman⁷). A is the acromial process, and B, the great tuberosity of the humerus. In a the arm is dependent at the side of the body, whereas in b it is slightly beyond horizontal abduction.

as pointed out by Codman, with consequent restriction of the normal range of motion at the shoulder joint.

Although these patients frequently exhibit neuritic symptoms, especially pain radiating down the upper extremity and up into the neck and back of the shoulder, the symptoms are not the result of a true neuritis, a term so frequently employed, but of the bursitis. Lack of an understanding of

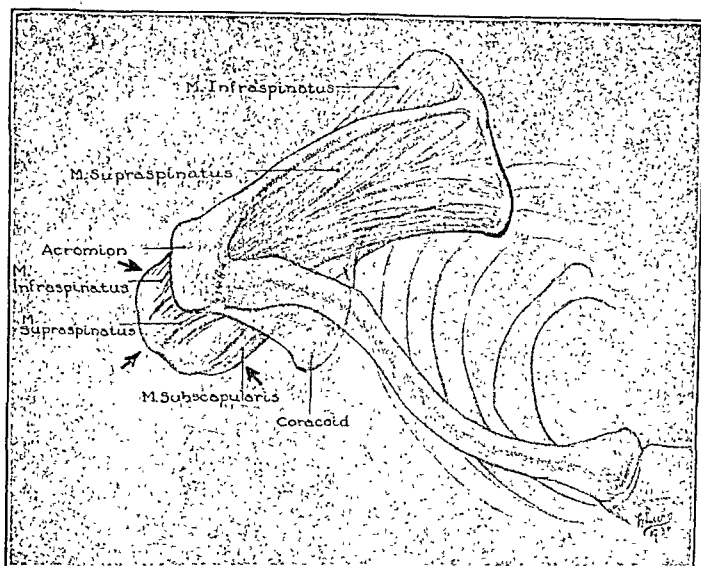


FIGURE 2. *Anatomical Drawing Made from a Dissected Specimen, Looking Down on the Shoulder from Above.*

This shows the origin and insertion of the short rotator muscles and their relation to the acromioclavicular joint. The subacromial bursa lies superior to these muscles, as shown in Figure 1.

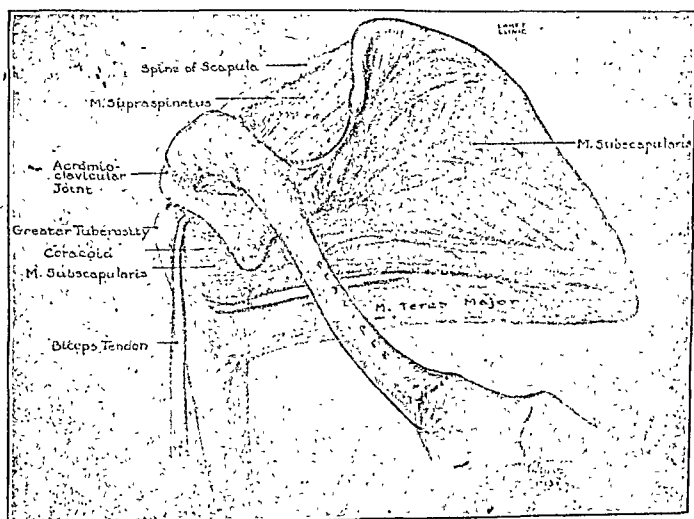


FIGURE 3. *Section of the Shoulder-Joint Region from Above and Anteromedially. This further illustrates the anatomy of the region.*

restoring normal shoulder function in this difficult group of cases.
When the patient is first seen, it is particularly

ment and active supervision of the case will obviously depend on many factors, such as the initial degree of limitation of shoulder function, the ex-

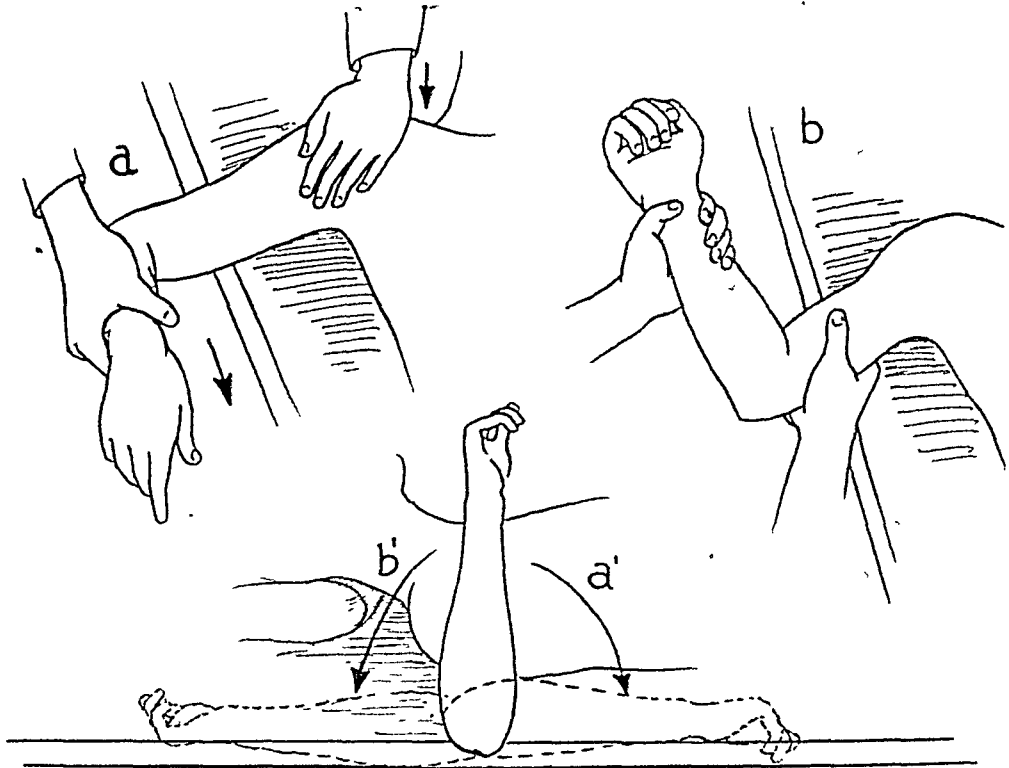


FIGURE 8. Manipulative Treatment to Obtain External and Internal Rotation.
As described in the text, these maneuvers are always done under general anesthesia, preferably intravenous Pentothal Sodium.

important that he clearly understand the basis of his disability, as well as the fact that it will require tent of muscle weakness and atrophy, the previous duration of symptoms and, especially, the pa-

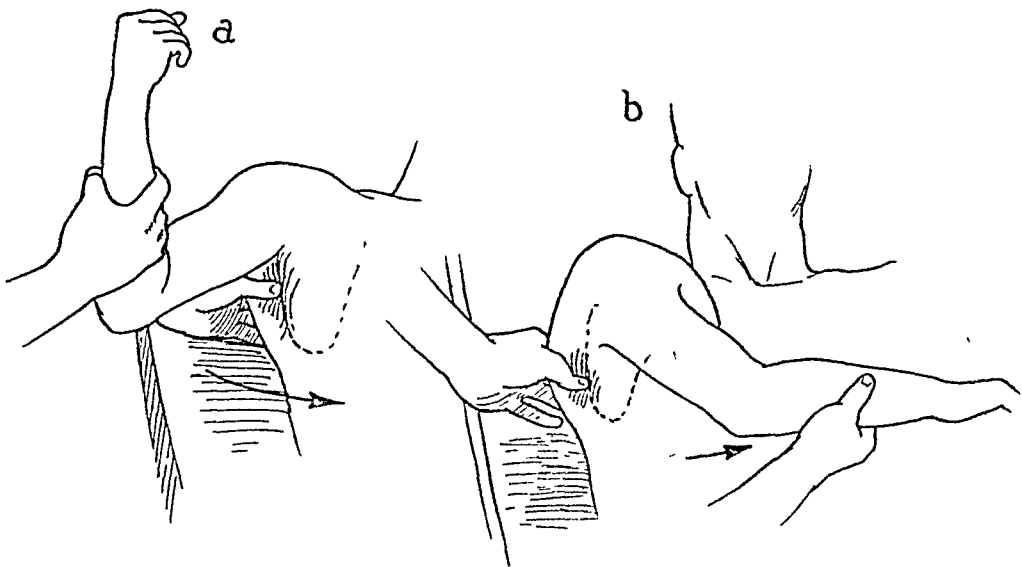


FIGURE 9. Manipulative Treatment of Chronic Adhesive Subacromial Bursitis.
This is designed to increase the range of adduction of the arm at the shoulder joint. Here again, immobilization of the scapula is necessary.

a minimum of three to four and occasionally as long as twelve to sixteen months to restore normal function of the shoulder. The actual extent of treatment's willingness to co-operate in the program outlined. The duration of treatment is emphasized because repeatedly patients who have had ade

quate therapy elsewhere but who did not realize the long period required to obtain normal function of the shoulder have become discouraged, have discontinued treatment, and have then sought advice from other physicians.

The patient also must understand clearly the significant role played by adequate and well-

rapid progress, not the least effect of which is the pronounced improvement in mental attitude.

Where considerable limitation of motion and marked discomfort exist, the patient is put to bed and the arm suspended in a Balkan-frame apparatus, with—and this is significant—the extremity in the maximum degree of abduction than

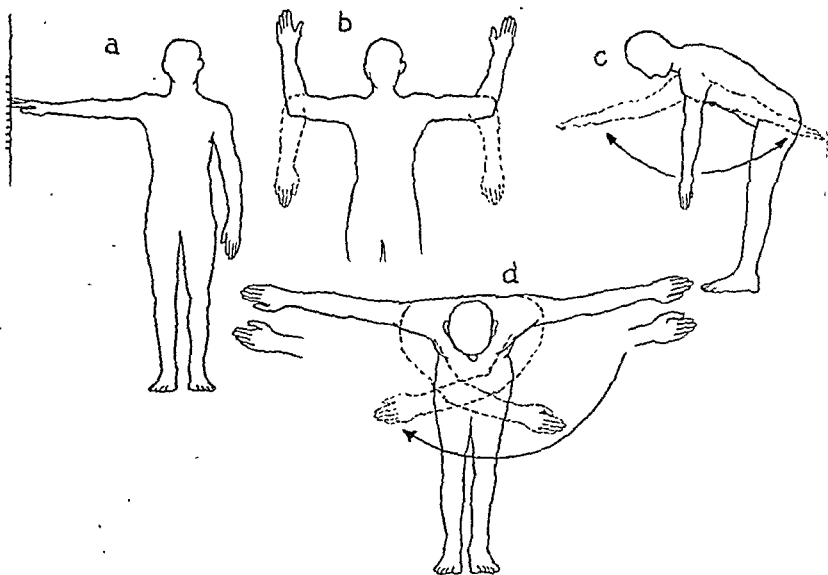


FIGURE 10. Diagrams of Exercises.

These are important in the ambulatory stage of the treatment of chronic adhesive subacromial bursitis. Note that the pendulum type of exercise permits what amounts to normal range of shoulder-joint motion without the effect of gravity and hence with a minimum degree of effort and discomfort.

directed physiotherapy. We particularly refer to progressive, active exercises of the shoulder musculature, carried out under the direction of a competent physiotherapist. This part of the treatment is performed at home by the patient, following initial training either in the clinic or in the hospital. Without exception all the patients with an adhesive bursitis require this phase of treatment.

On admission a patient with chronic adhesive subacromial bursitis is given the usual general examination, with particular reference to the local findings in the shoulder. Roentgenograms are taken and an analysis of the case is made. If the degree of limitation of motion is marked and the patient suffers considerable pain, he is advised to enter the hospital, since this permits much more

does not cause increased discomfort. Then adhesive traction, averaging 6 to 8 pounds, is applied to the upper arm, utilizing the Blake board. Intensive local heat repeatedly applied to the shoulder is instituted, together with massage. The patient is encouraged to move the arm in the apparatus as much as he can comfortably do so. Every effort is made to achieve general relaxation, to make the patient sleep well, and in general to establish the maximum degree of comfort possible under the circumstances. Such a phase may require as long as a week, but is oftener a matter of three to five days.

With the patient well adjusted to his apparatus, intensive active exercises of the shoulder are instituted. We have repeatedly observed that on this simple program the range of active and, in

particular, of passive abduction is increased as much as 30 to 40° in seven to ten days. When the patient has reached a maximum amount of improvement, as judged by his ability to abduct the arm, a shoulder-joint manipulation is carried

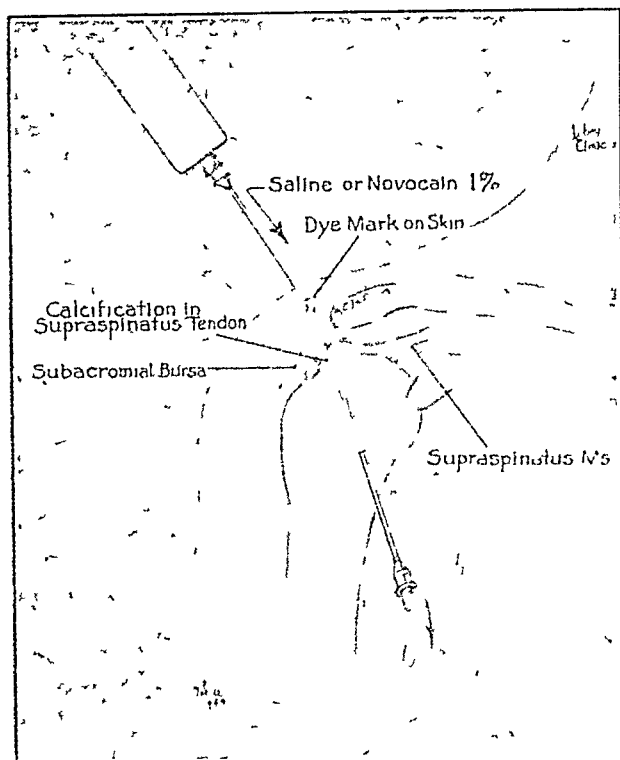


FIGURE 11. Removal of Calcified Deposits in the Tendon of the Supraspinatus Muscle.

This is accomplished by the "washing out" technic (Smith-Petersen¹¹). The dark area on the skin through which the superior needle has passed to enter the calcified deposit indicates the site of maximum tenderness on palpation. Localization by intermittent fluoroscopy permits accurate needling and washing out of the calcific material.

out under intravenous Pentothal Sodium anesthesia in the patient's room, with the arm in the apparatus.

Figures 7, 8 and 9 show the significant maneuvers in the actual manipulation. It should be noted that the scapula must be immobilized by one hand of the operator, while the other grasps the upper end of the humerus. In progressive stages the arm is moved laterally in abduction, during which maneuver numerous adhesions will be felt and heard to rupture. The significance of grasping the upper end of the humerus lies in the fact that this reduces the leverage action on that bone and hence it is less likely to fracture. No attempt is made to obtain a normal range of motion in the first manipulative procedure, because if this were done, frequently the resulting pain and discomfort would be so great that the patient would be unable to move the arm through the arc of mo-

tion that was present before the procedure. So in progressive stages the range of motion, both of lateral abduction and of rotation, is gradually increased. The actual extent of the manipulation is learned by experience, but a safe rule is to carry the arm through a lesser rather than a greater degree of motion.

With the manipulation completed, 1 per cent novocain is injected into the subacromial bursa, as well as into the periarticular structures of the shoulder joint. This idea, originally suggested by the work of Leriche and Policard⁹ in their treatment of sprains, has been of considerable aid in reducing the degree of discomfort that may follow the manipulation.

During the twenty-four hours after manipulation, no particular effort is made to have the patient move his arm unless he feels like doing so, but the intensive heat treatment is continued and sedatives are given as required to control discomfort. Beginning with the second postoperative day, active arm exercises are again instituted, in an attempt to increase the range of lateral abduction and of rotation. In practically every case the patient finds that he is able to move the arm through a wider arc of motion than was previously possible. Thereafter, the regimen as described is continued until further manipulation is indicated; this is performed after the patient again has reached a maximum degree of improvement.

As soon as the pain in the shoulder is less severe, the traction on the arm is progressively omitted, thus permitting much more active motion of the extremity. The patient then becomes ambulatory and begins pendulum exercises (Fig. 10), which are especially advantageous since the effect of gravity is eliminated and the patient can obtain normal motion at the shoulder joint with a minimum of effort. Likewise, in this same position the degree of pain caused by motion is considerably reduced.

In the ambulatory stage, the patient is discharged from the hospital and carries on his exercises at home, coming into the clinic on an average of two or three times a week for further physiotherapy, such as a combination of inductotherm, infrared radiation and massage, but always the main emphasis is placed on progressive active muscle exercises.

Thereafter the decision regarding further treatment depends on the patient's progress. If he is remiss in carrying out the active exercises and the adhesions recur, this negligence is emphasized, and he may then be readmitted for a few days in the hospital for further manipulative treatment. In the co-operative patient who continues under observation, however, this is usually unnecessary

A patient who lives at a distance is referred to his physician, and every effort is made to have him carry on treatment under the latter's active supervision.

In treatment of chronic adhesive subacromial

OPEN OPERATION

In one other group of patients, which includes two types, open operation is resorted to.

The most commonly encountered patient in this group is the one in whom the adhesions are

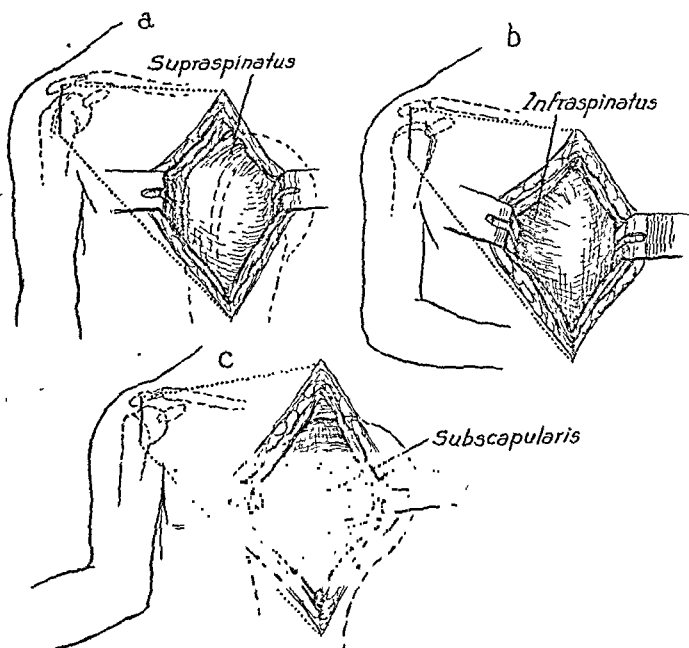


FIGURE 12. *Tendons of the Shoulder Joint.*

Through a small incision and with rotation of the arm, visualization not only of the subacromial bursa but also of the underlying tendons of the short rotator muscles is possible. The diagrams exhibit the tendons shown by the corresponding position of the arm.

bursitis with calcification in the bursa or in the tendon of the short rotator muscles, the foregoing program is also instituted with the following additions. The initial manipulation is done on the fluoroscopic table, again under intravenous Pentothal Sodium anesthesia. Needles are passed into the area of the calcification (Fig. 11), and as described in the article by Patterson,¹⁰ the technic of Smith-Petersen¹¹ is attempted—namely, the washing out of the calcified material. Before we were aware of this particular procedure, our practice had been to pierce the calcified deposit repeatedly with needles and inject novocain. This maneuver alone seems to encourage more rapid disappearance of the calcified deposit, but the washing-out technic has proved most efficacious.

so resistant to manipulative procedure that it is considered unwise to suture them. The bursa is therefore explored (Fig. 12) and many of the adhesions are divided with a knife, and thereafter the usual manipulative maneuvers are performed. It should be emphasized that the decision to open a bursa of this type is made because of the dense, firm adhesions in the presence of extensive bone atrophy. In such a patient the manipulations may well cause fracture of the shaft of the humerus. This possibility is eliminated by open operation, since a considerable number of adhesions are divided and those that remain in the less accessible part of the bursa can be ruptured by manipulation without fear of humeral fracture.

The other type of operative case is the one with a large mass of calcification that we have not succeeded in removing by the needling technic. Here the subacromial bursa is explored, and the calcified deposit as it lies in the tendon is incised and curetted out as described by Codman.

STATISTICS AND RESULTS

The data presented in this paper are based on an analysis of the treatment of 100 consecutive patients admitted to the Lahey Clinic because of chronic adhesive subacromial bursitis. Of this number, 9 patients, although improved on discharge, have not had an adequate follow-up for evaluation of the end results. Forty patients have been followed for over two years, 27 for over one year, and 14 for six months to one year. In 10 cases the follow-up was less than six months, but the results were so satisfactory that it was thought that an end result could be reported.

These 100 patients were divided into five groups. Those in Group A (47 cases) — were completely relieved of all symptoms and disability. Those in Group B (34 cases) were markedly improved. They had no disability and acknowledged only occasional pain. All the patients in Groups A and B returned to their previous occupations, and their ability to carry out these activities was in no way impaired. The patients in Group C (5 cases) were followed from six months to two years. All of them exhibited improvement but not enough to be classified in either Group A or B. Each of these 5 patients had either normal motion and some discomfort, or better than 50 per cent normal shoulder motion and no pain. The patients in Group D (5 cases) were unimproved. Those in Group E (9 cases) were improved on discharge, but the follow-up was inadequate.

Of 100 patients, therefore, the majority of whom were followed a minimum of six months and in most cases over a year, 81 either were relieved completely of all symptoms or were markedly improved and remained without any disability, although they occasionally complained of some shoulder discomfort.

SUMMARY AND CONCLUSIONS

In summarizing the treatment of this difficult

problem, we wish to emphasize the following significant points:

The patient should be forewarned regarding the basis for his disability and the considerable length of time that is often required to achieve a return of normal shoulder-joint function, as well as the absolute necessity for his complete co-operation in carrying out the often extremely fatiguing and boring exercises.

An initial period of bed rest, the arm in suspension and traction, usually results in marked increase of shoulder-joint function.

Manipulative procedures designed to break up the adhesions in the bursa and about the soft parts in the shoulder should be done in stages, and no attempt should be made to obtain normal motion in the shoulder at the first manipulation.

In the case of extremely resistant adhesions, especially when present in frail, poorly muscled patients who have had the loss of shoulder function for some time, with accompanying marked bone atrophy, it is preferable to explore the bursa, divide firm, fibrous bands, and eliminate the remaining adhesions by manipulation.

In chronic adhesive subacromial bursitis with calcification, the latter is removed by the washing-out technic or by open operation. Thereafter the regimen for patients without such deposits is carried out.

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A STUDY OF ERRORS IN THE DIAGNOSIS OF JAUNDICE*

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ON ward rounds and in clinicopathological conferences, cases with jaundice, especially those in the early stage, call forth a diversity of diagnoses and frequent mistakes. In the last six years 500 cases have come under our observation on the Second and Fourth (Harvard) Medical Services at the Boston City Hospital. These included most types of jaundice: complete and partial biliary obstruction, acute and subacute infectious and toxic hepatitis, the cirrhotics (portal, biliary, pigment, toxic and cardiac), fatty liver, tumors and syphilis of the liver and hemolytic jaundice. This paper is limited to 175 of these cases that came to operation or autopsy.

All known errors in diagnosis have been studied and classified. A statement of the number and kind of errors, showing which mistakes are commonest, may help to avoid them in the future. Errors are based on first-choice diagnoses only, and correct alternative diagnoses are not considered.

METHODS OF STUDY

In addition to a careful history and a general physical examination, special attention was paid to the size of the liver, spleen and gall bladder, the presence of ascites or spider angiomas, the icteric index, the color of the stool, tests for urinary diastase and the roentgenologic examination (Graham test, barium meals and enemas). Several liver-function tests were used in serial observations in each case, chosen from the following group: the excretion of urobilinogen and hippuric acid in the urine, galactose tolerance, excretion of bromsulfalein, the phospholipids, total cholesterol and cholesterol-ester percentage in the blood, the blood prothrombin level and its response to vitamin K, the serum albumin and the albumin-globulin ratio. In a small number of cases, peritoneoscopy and medical biliary drainage were used; biopsies of lymph nodes and liver were done when possible. A considerable number of the patients were followed and studied for months or years after the attack of jaundice in order to discover residual liver damage.

CLASSIFICATION

The cases were classified in four groups, as a guide to medical or surgical treatment: namely, complete biliary obstruction, partial biliary ob-

struction, hepatocellular jaundice‡ and hemolytic jaundice. McNee's¹ classification of jaundice was chosen as the most valuable clinical grouping, and obstruction was further divided, since it was found that complete obstructions were nearly all due to malignant neoplasms and partial obstructions were nearly all due to benign conditions. Rich's² classification into retention and regurgitation jaundice is important in showing the mechanism of jaundice, but has less clinical value than other classifications since there is rarely any difficulty in distinguishing these two types and since all the types of jaundice that are difficult to distinguish from one another are found in the regurgitation group.

The first two groups are essentially surgical with respect to treatment, and the last two essentially medical. The total group of 500 cases is listed in Table 1 to show the types. Almost one third of

TABLE 1 Cases of Jaundice Classified According to Type of Disease.

TYPE OF DISEASE	PROVED CASES	TOTAL NO. OF CASES	PER CENT
Complete external obstruction	29	33	6.6
Cancer of pancreas	20	24	
Cancer of common duct	6	6	
Cancer of hepatic ducts	2	2	
Stone in common duct	1	1	
Partial external obstruction	61	93	18.4
Gallstones	39	71	
Stricture of common duct	5	5	
Acute pancreatitis	4	4	
Cancer of bile ducts: pancreas or duodenum	5	5	
Cholangitis and abscess	8	8	
Hepatocellular jaundice	81	359	
Acute infectious hepatitis	9	101	20.2
Acute toxic hepatitis	2	41	8.2
Cirrhotics	41	161	32.2
Portal	30	127	
Piliary	2	9	
Pigment	2	7	
Tox	7	12	
Biliary (?)	6	3	
Cardiac	0	3	
Fatty liver	1	4	1.8
Tumor of liver	27	46	9.2
Syphilis of liver	1	1	0.2
Hemolytic jaundice	4	15	3.0
Totals	175	500	

the cases were chronic cirrhosis; about one third were toxic and infectious hepatitis; and about one third formed a group including gall-bladder disease, complete obstruction, tumors and syphilis of the liver and hemolytic jaundice. There was a surprisingly large proportion of cases of jaundice

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to injury to liver cells

to injury to liver cells

due to cirrhosis. The patients evidently enter the hospital when there is an attack of acute hepatic necrosis or decompensation. The percentage is greater in this hospital group than in the cases encountered in private practice.

In Table 1 are also listed 175 proved cases that came to operation or autopsy.

In Table 2 are given the proved errors in these 175 cases. They are classified in groups, with the correct diagnoses in one column and the erroneous diagnoses in the next column.

The proved errors in the 175 cases that came to operation or autopsy totaled 14, or 8 per cent. Needless to say, in many cases of jaundice that were easiest to diagnose the patients did not die and were not operated on. These included patients with acute toxic and infectious hepatitis

TABLE 2. *Erroneous Diagnoses in 175 Cases with Operation or Autopsy.*

TYPE OF DISEASE	CASE No.	ERRONEOUS DIAGNOSIS	CORRECT DIAGNOSIS
Complete obstruction	1	Cancer of common duct	Gallstones
Partial obstruction	2	Chronic genito-urinary infection	Cholangitis, abscess of liver
	3	Cirrhosis	Cancer of duodenum
	4	Cirrhosis	Primary cancer of hepatic ducts
	5	Cholangitis	Primary cancer of common duct
Hepatocellular jaundice:			
Acute hepatitis	6	Obstruction	Subacute yellow atrophy
Cirrhosis	7	Portal cirrhosis	Pigment cirrhosis
	8	Portal cirrhosis	Pigment cirrhosis
	9	Biliary cirrhosis	Portal cirrhosis, cholecystitis
Tumor of liver	10	Cirrhosis	Secondary cancer of liver (breast)
	11	Cirrhosis	Secondary cancer of liver (pancreas)
	12	Cholangitis	Secondary cancer of liver (esophagus)
	13	Possible cardiac cirrhosis; infarcts	Secondary cancer of liver (stomach)
Hemolytic jaundice	14	Hepatorenal syndrome	Arteriosclerotic heart; infarcts of lungs and spleen; passive congestion.

-and hemolytic jaundice and many with chronic cirrhoses who had been under observation at the hospital for a long time, so that the actual percentage of erroneous diagnosis in the whole group was probably somewhat less than that given above.

KIND OF ERRORS

The known errors were in the chronic cases, with a single exception, a case of subacute yellow atrophy (Case 6).

Complete Obstruction

One case was diagnosed as cancer when it was absent, on the basis of complete obstruction of the

biliary passages. A man of fifty-two (Case 1) with a history of increasing painless jaundice for two months and a final icteric index of 100, gray stools and entire absence of urobilinogen in the urine on daily tests over a period of ten days showed at operation gall-bladder disease, with the hepatic and common ducts solidly plugged with puttylike material and gravel, causing complete obstruction.

Partial Obstruction

A man of seventy-seven (Case 2) with a known chronic genitourinary infection, pyuria, pyelitis and prostatic abscess also had empyema of the gall bladder, cholangitis and multiple liver abscesses, with slight obstruction of the biliary passages. The jaundice was slight and lasted only two days. The genitourinary infection masked the biliary-tract infection, which was not recognized.

A man of sixty (Case 3) of alcoholic habits had continuous deep, painless jaundice for six weeks, a large firm liver, a high urobilinogen falling to normal, stools yellowish to gray and possible slight ascites. Barium x-ray films were normal. It was difficult to decide between terminal chronic hepatitis with loss of function and partial external obstruction. A diagnosis of portal cirrhosis was made. The autopsy showed a primary cancer of the duodenum that gradually involved the ampulla and pancreas and that was missed by the roentgen ray, with a few metastases in the liver. The partial obstruction that was present when the diagnosis of cirrhosis was made became complete in the last two weeks of life, with clay-colored stools and absence of urobilinogen in the urine.

A fifty-one-year-old man (Case 4), moderately alcoholic, had dull pain in the region of the right scapula, deep jaundice for one week, slight hematemesis and a little irregular fever. The liver was slightly enlarged. There was a question of a palpable spleen and some ascites. The stools were light brown, the urobilinogen in the urine was increased (positive on four occasions in dilutions of 1:32, 1:16, 1:64 and 1:4 respectively), and roentgen-ray examination of the stomach and bowel was normal. The patient continued to be deeply jaundiced for two months and died in coma. A diagnosis of portal cirrhosis was made, with latent carcinoma causing partial obstruction as the second choice. Autopsy showed primary carcinoma, partially blocking both hepatic ducts, with metastases in the liver, lungs and adrenal glands.

A woman of seventy-six (Case 5) with an unusual small, soft adenocarcinomatous polyp in the common duct had epigastric pain, chills and irregular fever, moderately deep jaundice, some increase in the size of the liver, bile pigment in the

stool and increased urobilinogen in the urine, and was considered to have partial obstruction of the common duct due to stone, with infection of the bile passages and liver. At autopsy, in addition to the polyp in the common duct, there was extensive cholangitis with multiple abscesses of the liver.

Hepatocellular Jaundice

Acute hepatitis. A sixty-year-old man (Case 6) had two weeks of painless, steadily increasing deep jaundice (icteric index 100 to 200), complete absence of urobilinogen in the urine for ten days and normal galactose-tolerance tests. The diagnosis wavered between subacute hepatitis and obstruction of the common duct, and the patient was finally operated on. A longer period of observation and tests might have avoided this mistake. At autopsy, a healing acute yellow atrophy was found.

Cirrhosis. Two cases of pigment cirrhosis (Cases 7 and 8) were called portal. Neither patient had external pigmentation or glycosuria, and both were hard drinkers. One case of portal cirrhosis (Case 9) with accompanying cholecystitis was diagnosed as biliary cirrhosis.

Tumors of liver. Cancer was overlooked in 4 cases. Two of these patients had secondary cancer of the liver from a tiny primary focus, which caused no symptoms whatever and was discovered only at autopsy. One patient (Case 10) had a nodule in the breast the size of a small pea, and the other (Case 12) had a tiny nodule in the esophagus.

One patient (Case 11) had a latent cancer of the body of the pancreas not involving the common duct, with massive secondary cancer of the entire liver.

In 1 patient with chronic decompensated valvular heart disease (Case 13), the roentgen-ray examination of the stomach was unsatisfactory on account of weakness and vomiting. A cancer was suspected but not proved. Actually a medium-sized prepyloric cancer was present, with massive involvement of the liver.

Hemolytic jaundice. In a case of acquired hemolytic jaundice the diagnosis failed. A man of forty-one (Case 14) with chronic arteriosclerotic heart disease developed deep jaundice after ten days in the hospital (icteric index 40 to 100). He had multiple venous thromboses from venipuncture for the use of Mercupurin, signs of multiple infarcts in the lungs, moderate uremia (anuric for one day, with the nonprotein nitrogen 70, 82, 50, 60 and 30 mg. per 100 cc. in five successive samples of blood), some bile in the urine and evidence of liver damage (the urobilinogen in the urine rising and remaining positive in a dilution of 1:128). The liver was 2 to 3 cm. below the costal margin.

The vague diagnosis of hepatorenal syndrome was made on the basis of combined hepatic and renal damage. The autopsy showed, in addition to the above, infarcts in the spleen, a pathologic gall bladder containing two stones, with the large patent bile ducts, and passive congestion of the liver and kidneys. This confusing picture of multiple disease was dominated by hemolytic jaundice from the multiple infarcts in the lungs and spleen, to which insufficient attention was paid.

DISCUSSION

Errors of Diagnosis

Of 29 proved cases of complete obstruction, 28 (97 per cent) were due to cancer, and of 61 proved cases of partial obstruction of the common or hepatic ducts, 56 (92 per cent) were due to benign conditions. The 5 cases of cancers with partial obstruction of the external biliary passages comprised the following: 1 case (Case 3) of cancer of the duodenum with extension to the pancreas in which partial obstruction became complete in the last two weeks of life, 3 cases of almost complete obstruction—namely, 2 cases of cancer of the head of the pancreas correctly diagnosed and 1 (Case 4) of cancer of the hepatic ducts—and 1 unusual case (Case 5) of a soft pedunculated adenocarcinoma of the common duct 1 to 2 cm. in diameter.

The presence of complete obstruction with continuous absence of bile from the feces and of urobilinogen from the urine has strongly favored the diagnosis of cancer involving the common duct (in the head of the pancreas, the ampulla of Vater or the common duct) or both hepatic ducts. When a cancer obstructs the common duct and has caused well-marked jaundice, it usually does not take long to produce complete obstruction, judged by the continued absence of urobilinogen from the urine with the Wallace and Diamond³ test or a very low figure (0 to 0.3 mg. daily) with the Watson⁴ test.

One case (Case 1) of complete obstruction of the common duct was diagnosed as a cancer when it was stone. This mistake was not important except for the prognosis, since, in either event, surgery was required.

There was a great difference in the importance of the errors in the various groups. The error was most serious in Case 6, in which a patient with acute hepatitis was operated on for obstructive jaundice and died of bronchopneumonia, and was found to have a healing subacute yellow atrophy. This case was encountered six years ago; this mistake has not been repeated, and we have had several opportunities to restrain sur-

geons from exploring other patients at an early stage of the disease.

The determination of the cause of the jaundice in the first day or two of the disease is not essential since these are not emergency cases. In acute deep jaundice a short period of study is especially needed to avoid operating early with a diagnosis of complete or partial obstruction without adequate knowledge of the liver function or the surgical risk and course of the jaundice and without making the best diagnosis possible. A good rule in acute deep jaundice with brown stools is to avoid surgical treatment. The disease is obviously not due to external obstruction, but chiefly or entirely to damage of the liver cells (acute hepatitis, cirrhosis with acute necrosis and so forth). The risk of operating for severe or acute diffuse hepatitis at the height of the jaundice is extremely great. This is seen when the mortality of ordinary gall-bladder operations, from 2 to 5 per cent, is compared with that of about 35 per cent in operations on cases of cirrhosis and with one of nearly 100 per cent in operations on cases of acute yellow atrophy or severe acute hepatitis. In acute jaundice it was often a serious question how long to wait to watch the course of the disease. In acute cases without obvious infection and pain (acute hepatitis, necrosis in cirrhosis, obstruction by stone or hemolysis), the danger lies entirely on the side of early operation in cases with a wrong diagnosis. In chronic cases there is no reason to hurry a difficult diagnosis. Most patients with obstruction due to stone preserve good liver function for a long time, and other cases are either unsuitable (cirrhosis) or unsatisfactory (cancer) for surgery.

Too many diagnoses of cirrhosis were made when latent cancer was present, chiefly because the patient was a steady drinker and had a deficient diet and enlarged liver. The large majority of steady drinkers (over 90 per cent) never develop cirrhosis. Various cases of cancers were called cirrhosis, but no case of cirrhosis was called cancer. The best differentiation is achieved through the history and physical examination, but ascites may occur in both diseases and a palpable spleen may be absent in both.* Liver-function tests usually show some damage in both. This is more marked in well-developed diffuse cirrhosis than when nodules of cancer are scattered through a normal liver, on account of good compensation of the latter.

It is easy to confuse portal cirrhosis with the toxic cirrhosis that follows an attack of subacute yellow atrophy of the liver (Mallory⁵) when the acute attacks of the latter are not striking or

occurred so long ago that they have been forgotten. Erroneous diagnosis of cirrhosis, such as calling pigment cases portal, is of minor importance, since the treatment is similar for both—namely, medical.

There was 1 proved case of primary cancer of the liver (hepatoma) in the 41 cases of cirrhosis that came to autopsy. This is rarely discovered clinically, but is chiefly diagnosed pathologically.

Over half the proved errors—namely, 8 out of 14—were associated with cancer. One case (Case 1) was diagnosed as cancer because of complete biliary obstruction; cancer, however, was absent.

Cancer was overlooked in 7 cases. Of these, 4 (Cases 3, 4, 10 and 11) were called cirrhosis, 2 (Cases 5 and 12) were called infections of the liver (cholangitis with multiple small abscesses), and 1 (Case 13) was diagnosed as chronic passive congestion of the liver with possible infarcts in a patient with decompensated rheumatic mitral and aortic disease of long standing. These 7 cancers were difficult to find clinically. In 1 case primary cancer of the duodenum (Case 3) was missed by the roentgen ray. Cancer was primary in the bile passages in 2 cases, in the common duct in 1 (Case 5) and in the hepatic duct in 1 (Case 4). In 4 cases it was secondary—arising in 2 from tiny foci in the breast (Case 10) and esophagus (Case 12), in 1 (Case 11) from a latent cancer of the body of the pancreas and in 1 (Case 13) from a cancer of the stomach in a patient too weak for examination. These 7 cases of latent cancer within the liver or bile passages were extremely serious, with no opportunity for palliative surgical treatment, which in some cases was useless and in others was impossible because of the poor condition of the patient. Fever and leukocytosis in late cancer may simulate cholangitis and liver abscess. Probably an error in diagnosis can be avoided by a more frequent consideration of the possibility of cancer.

Multiple lesions were sometimes confusing. The symptoms of one lesion overshadowed those of another, as in Case 2, in which an obvious genitourinary infection covered the signs of a latent but extensive infection of the biliary tract. In Case 13, a patient with a chronic valvular heart disease showed well-marked symptoms, whereas the cancer of the stomach and liver were only vaguely suspected. In Case 9, the cholecystitis was easily diagnosed but the portal cirrhosis was latent.

Ease of Diagnosis

There was a great difference in the ease of diagnosis of the different diseases. The easiest

*The methods of diagnosis will be discussed in a later paper

to diagnose was toxic hepatitis in which there was a history of exposure to arsenic, cinchophen, chloroform, carbon tetrachloride, gold thiosulfate or some other drug and in which no mistakes in diagnosis were made. Patients with toxic cases may have multiple diseases such as syphilis and asphenamine hepatitis, with alcoholic cirrhosis or cancer.

The disease next easiest to diagnose was complete obstruction, which was apparent on the basis of absence of bile in the bowel, determined not only by the color of the stools but better still by the complete absence of urobilinogen from the urine on repeated tests. All but 1 of these cases were cancerous.

Hemolytic jaundice had so many distinctive features that with careful study the diagnosis was usually easy. In chronic familial cases, the history, lack of pain, anemia, low-grade icterus, splenomegaly, small spherocytes, increased fragility of the red cells, presence of reticulocytes, lack of bile in the urine (usually), an excess of bile pigment in the feces and an indirect van den Bergh's reaction in the blood are distinctive. The presence of bile in the urine does not rule out hemolytic jaundice, since in some cases there is accompanying liver damage, apparently due to anoxemia (anemia, heart disease, pneumonia and so forth).

The sudden appearance of jaundice in patients with chronic myocardial insufficiency should make one suspect pulmonary infarct as a cause of the jaundice, even without local signs (Keefer and Resnik⁶).

The diagnosis of gall-bladder disease is relatively easy with modern methods,—the history and physical examination combined with Graham tests, biliary drainage and so forth,—as was also the diagnosis of acute pancreatitis with the additional help of early tests of the urinary diastase. Some patients were too sick for thorough examination, and this proved to be a source of error, as in Case 13.

Diagnosis of cancer of the liver was easy following previous operation for cancer of the stomach, bowel, prostate, pancreas and so forth or by biopsy of a lymph node, but the most difficult cases for diagnosis were those of small or latent cancer of the liver and common or hepatic ducts, which were not always distinguished from cirrhosis and cholangitis.

There are several small groups of cases in which no error in diagnosis was made that is worth mentioning.

Only 8 cases were classified as simple fatty liver; in 1 of these an alcoholic patient developed pneumonia and died. The autopsy showed a

large, soft, fatty liver without cirrhosis. In the other proved cases the fatty livers were complicated by cirrhosis. Unproved cases with two or more of several clinical signs—a much enlarged liver, jaundice, ascites, an enlarged spleen, varices, a low serum albumin, low prothrombin, edema, hemorrhages and poor liver function—were classified as fatty portal cirrhosis.

There were only 4 cases of acute pancreatitis with jaundice, all correctly diagnosed and all associated with gallstones. The diagnosis was relatively easy with the combination of jaundice, severe epigastric pain, vomiting, leukocytosis and, especially, marked increase of urinary diastase (in dilutions of 1:300, 1:1600, 1:2200 and 1:7500, respectively). No diagnosis of chronic pancreatitis was made, and no case was discovered at operation or autopsy.

Syphilis of the liver was proved in only 1 case (0.6 per cent) in the group of 175 jaundiced patients who came to operation or autopsy, and was not diagnosed again in the total series of 500 cases. A man of seventy had been explored thirty-five years previously at another hospital for an abdominal tumor, which proved to be a gumma of the liver with adhesions to the stomach. Treatment was inadequate. When he entered this hospital because of dull pain in the right upper quadrant of the abdomen, the jaundice was slight (icteric index 13), the liver was large, firm, irregular and tender, a blood Hinton reaction was negative, there was no ascites, and liver-function tests were almost normal. Peritoneoscopy was unsatisfactory because of omental adhesions to the liver. The reported incidence of syphilis of the liver has gradually lessened in recent years, probably as a result of earlier and better treatment.

Weil's disease (spirochetosis icterohemorrhagica) was not diagnosed or found post mortem in this series. It is evidently rare in this region, but the apparent rarity may be due in part to the fact that the clinical picture and laboratory methods are not well known. If earnestly looked for by means of proper bacteriologic procedures in cases of acute infection or catarrhal jaundice, cases will occasionally be recognized.*

SUMMARY AND CONCLUSIONS

The proved errors in diagnosis in 175 cases of jaundice that came to operation or autopsy was 14 (8 per cent).

The known errors, with one exception, were in the chronic group, and over half the errors were associated with the diagnosis of cancer, almost always in overlooking small or latent tumors.

*Three cases were found on other medical services at the Boston City Hospital in the last five years.

It is evident that latent cancer should be considered much oftener in doubtful chronic cases. There was a tendency to make too many diagnoses of portal cirrhosis in alcoholic patients with an enlarged liver. Various cancers were called cirrhosis, but no case of cirrhosis was called cancer.

Complete obstruction of the external bile ducts was due to cancer in 96 per cent of the proved cases, and partial obstruction was benign in 91 per cent.

The essential need is to separate medical from surgical cases of jaundice. This is far more important than is the diagnosis of the specific disease of the liver; for example, it is far more important to differentiate hepatitis, the treatment of which is essentially medical, and complete obstruction, in which it is essentially surgical, than to decide just which kind of cirrhosis or complete obstruction is present.

Cases of jaundice are rarely emergencies, and it is best not to hurry the diagnosis in most acute or chronic cases, especially in the absence of serious infection (cholangitis, abscess of the liver, empyema of the gall bladder, perforation or peritonitis), and not to trust to early impressions, which are often reversed by the course of the illness and the laboratory tests. It is especially necessary not to make the early diagnosis of acute deep jaundice a basis for early surgery, which in this series had a high mortality in the wrongly diagnosed cases. A period of study, with the giving of plenty of glucose and water, protein and vitamins, is essential in order to watch the course of the disease and to see which element predominates—damage to the liver cells, external obstruction or hemolysis.

If unexplained jaundice appears in chronic heart

disease, pulmonary infarct or hemolytic jaundice should be considered.

The ease of diagnosis of jaundice was approximately in the following order. The diseases easiest to diagnose were toxic and infectious hepatitis, complete external obstruction and hemolytic jaundice. Those moderately difficult to diagnose were fatty liver, acute pancreatitis, gall-bladder disease with partial external obstruction and cirrhosis. The most difficult to diagnose were multiple lesions, cases in which the patients were extremely sick and had incomplete examination and tumors of the liver and bile passages.

The differentiation of hepatocellular and obstructive jaundice and of stone from cancer in the common duct has become easier in the last ten to twenty years, but the difficulty of discovering various latent cancers causing jaundice remains.

Syphilis of the liver is less common than in the past, there having been only 1 proved case. No cases of Weil's disease or chronic pancreatitis were diagnosed or found.

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MEDICAL PROGRESS

INDUSTRIAL HYGIENE

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FOR the first time in the history of the United States, its manpower has been found to have quantitative limits. Since this commodity cannot be rapidly expanded, human resources must be husbanded; and since industrial hygiene is concerned with the preservation and improvement of the health of the worker, it has assumed a greater importance than heretofore. Conspicuous advances have been made not only in the prevention of specific occupational hazards, but also in the development of the public-health viewpoint in industry with the worker as the chief recipient of its benefits.

The application of newer knowledge in industrial hygiene has been constantly expanded under the stimulus of federal funds, which have since 1936 been aiding state industrial-hygiene activities. At the present time, there are approximately forty-seven units in thirty-eight states with about three hundred active workers.¹ Co-operative arrangements between these state units and other agencies responsible for worker health have been effective in spreading the recent gains in industrial hygiene.

SPECIFIC OCCUPATIONAL HAZARDS

The war has introduced a host of new chemicals of relatively unknown toxicity, besides accelerating the use of the numerous substances about whose toxicity much is known. Modern industry rests on a chemical base, and its constant development continuously creates new problems in industrial hygiene. Some of these are of temporary nature, but many will continue into the postwar world.

The Pneumoconioses

The pneumoconioses are still a fruitful source of medical investigation, since many points about them are still to be defined. The roentgenologic picture has been thoroughly reviewed by Pendergrass,² who has admirably summed up the difficulties and variations in the x-ray interpretation

of occupational disease of the thorax. It has been customary to think that the only disabling pneumoconioses are those due to silica and asbestos. Recent investigations, however, create the belief that the list will have to be expanded to include such silicates as talc and mica, and the literature abounds in cases of pneumoconioses from various minerals and earths.^{3,4}

Porro et al.⁵ presented 15 cases of talc pneumoconiosis, including 5 autopsies, and in 13 of these the disability was directly attributable to the pneumoconiosis. Talc dust varies greatly mineralogically, and the highest incidence occurs in those workers exposed to talc with a high percentage of tremolite.⁶ Mica, another silicate, has given rise to an incidence of lung fibrosis of 11.4 per cent in miners of this mineral.³

Certain dusts such as coal and aluminum have not only been called harmless but are stated to have an antidotal effect. More recent investigations, however, indicate that these substances are not entirely harmless and may in fact cause some degree of pulmonary fibrosis. Anthracosilicosis is rather frequent, as recent surveys have proved.^{7,8} The dangers to the lung from aluminum have been discussed in the German literature. It is stated that aluminum dust must be included in the list of pneumoconiosis-producing substances, although it remains to be proved whether it produces specific lesions.^{9,10} On the other hand, Crombie and Blaisdell¹¹ report encouraging results from the symptomatic treatment of silicosis with aluminum dust and believe that it is an effective preventive. Silica is soluble to about 200 parts per million, and a small amount of metallic aluminum is stated to reduce this solubility to about 6 parts per million.

The study of the pathology of silicosis has continued. It has always been defined as a local disease of the lungs and thoracic lymph nodes. Recently a case came to autopsy that also showed systemic dissemination of silicotic nodules in the liver and spleen.¹²

Engineering methods of dust control have progressed to the stage that, in most industries, no worker need be exposed to a hazardous concentration of any pneumoconiosis-producing dust.

A number of new pulmonary syndromes have

The articles in the medical progress series of 1941 have been published in book form (*Medical Progress Annual*, Volume III, 678 pp., Springfield, Illinois: Charles C. Thomas, 1942, \$5.00).

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recently been described, and a fairly definite one, called "bagassosis," has been reported from the English literature. This lung disease is due to dust created by the crushing of broken sugar cane after the sugar has been extracted. Many exposed to this fine dust become sensitized and after several months develop dyspnea, cough, weakness and anorexia. The illness is severe and prolonged, but recovery ultimately takes place. The x-ray picture is similar to that of an inflammatory condition. Cases have recently been reported as having occurred in Louisiana, where a similar process is in operation.^{13, 14}

Another interesting lung disease has recently been reported in persons working in beryllium-recovery plants.^{15, 16} This pulmonary condition is characterized by dyspnea, cough and low-grade fever. The illness usually lasts about three months, and the x-ray picture suggests a diffuse inflammatory inhalation reaction. Practically all the affected workers recovered, but there have been a few fatalities. A group of cases similar to these have occurred recently among workers engaged in making electrical equipment and lamps.¹⁷ This condition is characterized by dyspnea and cough, weakness and loss of weight. The illness runs a more chronic course. One autopsy demonstrated the pathological findings of sarcoidosis. The x-ray picture is consistent with this diagnosis.

Lead

Lead, historically the most ubiquitous hazard to industrial health, is today being met with ever more frequently, and often in quite new roles. Although the usual industrial uses, as in foundries, paint making and storage-battery manufacture, continue to contribute their quotas of lead poisoning, many salvage operations coming to the fore, such as the oxyacetylene cutting of steel, which has been previously covered with lead paint, are proving highly dangerous.¹⁸ Fatal cases of encephalopathy occurring from inhaling fumes from storage-battery boxes burned as fuel have been reported.¹⁹ Such engineering aids as ventilation and wet mining methods have, however, helped to cut down the high incidence of lead poisoning in a number of industries.²⁰ The factors involved in the industrial exposure have received further attention, and the standard of 1.5 mg. per 10 cu. m. of air has been well substantiated as the upper limit of tolerance.

Experimentally, investigation has been going on regarding the behavior of lead in body tissues. The behavior of lead in the organism as a whole is dependent on the mechanism of its storage in the body, and means of identification in body tissues

have been perfected by Fairhall and others. The dropping mercury electrode and the development of radioactive lead as an indicator give promise of greater advances to come.²¹⁻²⁵

The therapy of lead poisoning is still not entirely clarified. In the past, ascorbic acid was suggested as a means of increasing the lead excretion,²⁶ but clinical observation has not proved that this vitamin has any effect on increasing the excretion of lead from the body.²⁷ The value of milk is somewhat controversial, but there is growing evidence that a person with a positive calcium balance retains less lead. Although milk cannot be considered the keystone of any preventive or therapeutic regime, it is of value in workers exposed to this hazard.

The physical signs and symptoms of lead poisoning have been thoroughly reviewed in articles by Kehoe²⁸ and Ashe.²⁹ Lead poisoning is primarily a clinical syndrome. Diagnosis is helped by study of the excretion, but the final diagnosis depends on an interpretation of clinical symptomatology, which affects chiefly the gastrointestinal and neuromuscular systems. Elimination of ingested lead is accomplished spontaneously, even without "de-leading." Gross changes in the acid base balance or calcium-phosphorus metabolism of the body are not affected if the lead exposures are kept within tolerance limits.³⁰

Control of the lead hazard has been aided in several states by the development of a health-department laboratory service similar to the Wassermann service offered by many states. Lead-free kits are distributed to physicians for the transmission of samples through the mails. This technic has not been adopted universally as yet, but has promise of further development as the medical profession becomes aware of the increasing incidence of lead poisoning.^{31, 32}

Miscellaneous Chemicals

An ever greater variety of miscellaneous toxic chemicals are finding use in industry. The two groups that have been especially studied because of their widespread application and particular necessity in wartime are those compounds that are used as solvents and those used in the making of munitions. The general use of benzol as a solvent has decreased somewhat as manufacturers have become increasingly aware of its toxic qualities. Some of its industrial uses are, however, still widespread; but fortunately many of these processes are carried out in closed systems, and hence no fumes are liberated under usual operating conditions.

The group of compounds known as chlorinated hydrocarbons are extensively used as degreasers

and as solvents. Carbon tetrachloride, although still widely used, has yielded in many instances to trichloroethylene. This latter substance, while less toxic, can cause serious effects and there is an unjustified complacency about its use.³³ The maximum allowable limit in workroom air is 200 parts per million, twice the figure hitherto accepted for carbon tetrachloride, since it is excreted fairly rapidly as trichloroacetic acid after detoxification in the body.³⁴ The symptoms of an excess inhalation of this substance are dullness, nausea, vomiting and coma. Reports in the literature still demonstrate the menace of carbon tetrachloride, which in acute poisoning gives rise to liver and kidney damage, coma and death; it is urged that the maximum allowable limit of this compound be revised drastically downward, since numerous cases of nausea and headache have occurred among workers exposed to less than 100 parts per million, the figure until recently thought to be safe.³⁵⁻³⁷

Ethylene dichloride, also a chlorinated hydrocarbon, is now used as a rubber solvent. Its toxicity is not completely defined, but apparently it too can cause nausea, vomiting and liver damage. Experimentally, it produces an irritation of the eyes in low concentrations. The present maximum figure of 200 parts per million may have to be revised downward.

Toluene has in many instances replaced benzol as a solvent. Although less toxic, it nevertheless can produce hepatomegaly, macrocytosis, a moderate secondary anemia and an absolute lymphocytosis. These changes may occur without any symptomatology. Hence, power ventilation is often necessary where toluene is used.³⁸

Munitions making is still quite hazardous to health, but ventilation procedures have greatly reduced these dangers. No special advance has been made in the medical knowledge of poisoning by trinitrotoluol (TNT), the maximum allowable limit for which has been set at 1.5 mg. per 10 cu. m. of air. Tetryl, a common explosive, is a potent source of dermatitis, and there is some evidence that it may be a systemic toxin. The dermatitis is characteristic, as is the yellow staining of hair and skin.³⁹ Detonators and "boosters" in munitions making, such as lead azide and mercury fulminate, are toxic when inhaled or absorbed. Fortunately, exposures to both these substances are well controlled, since they are most dangerous from the explosive standpoint.

The hazards associated with welding have been more clearly defined. Metal-fume fever, which occurs when zinc and other metallic oxides are inhaled in sufficient quantities, has been shown to be a well-defined syndrome.⁴⁰ It is characterized by chills, fever and leukocytosis several hours after the exposure, clearing up without sequelae

within a day or so. This exposure, as well as those to carbon monoxide, nitric oxide fumes, fluorides and other materials used in the welding fluxes, may usually be controlled by adequate power ventilation.⁴¹

Mercury and Radium

Since December, 1941, no mercury-carroled fur has been used in the making of felt hats. This has resulted in a decrease in the incidence of chronic mercurialism. Occasional cases are still reported from other industries, and mild cases have been known to occur among physicians and chemists exposed to mercury during laboratory procedures. This hazard is not generally recognized, but since mercurialism may result either from ingestion, inhalation of vapor or absorption through the skin, it is not uncommon where mercury is carelessly handled.

The best guide in chronic industrial poisoning is determination of the urinary excretion, since little or no mercury is normally found in the urine except in persons with a recent amalgam filling or in cases where a mercurial antiseptic has been used.⁴² Standards for atmospheric contamination have been evolved, and the American Standards Association has accepted 1 mg. per 10 cu. m. of air as the maximum allowable limit.⁴³ The mining of mercury is still hazardous, but the incidence of mercurialism has been kept down by the use of a new chemical spray in the mines. This consists of a lime-sulfur mixture with a suitable wetting agent. When sprayed on the working surfaces of the mine, it reduces the volatilization and has proved effective in conjunction with good house keeping.⁴⁴

The necessity for employing self-luminous compounds on the dials of instruments used in combat vehicles has intensified the industrial use of radioactive substances. The expansion in terms of number of workers has increased over fifty-fold, but the hazard of radium poisoning has fortunately this time been recognized and extensive measures have been taken to prevent it. A number of states have promulgated codes designed to prevent the ingestion or inhalation of abnormal amounts of radium. The development of extremely sensitive physical methods of determining the amount of radium stored in the body has helped greatly as a guide to prevention. One tenth of a microgram of radium has been established as the maximum permissible storage limit. So far, no cases of radium poisoning have been reported, and it is hoped that the preventive measures now instituted will obviate the occurrence of cases similar to those that followed the last war.⁴⁵⁻⁴⁹

DERMATOSES

Dermatitis continues to be one of the major problems confronting the industrial physician and, in terms of morbidity, is the greatest single factor contributing to absenteeism from illness. Dermatitis as a result of contact with the cutting oils used in machining operations is still the most frequent type. No one method of control is adequate, but effective preventive measures center in personal protective devices and proper methods of cleansing the skin. Protective clothing and protective creams are helpful in minimizing contact, and these, together with hot water, a good soap and frequent bathing, greatly reduce the hazard. Harsh abrasive mixtures and strong solvents must be avoided. The use of clean oil helps to keep down the incidence of oil pimples, but sterilization of reused oil, either by chemicals or heat, is not indicated, since infection is produced by organisms normally present on the skin.⁵⁰

Dermatoses due to a host of sensitizing and allergic agents are of common occurrence, and almost any substance used in industry may cause a rash. Such conditions cannot be adequately prevented by pre-employment patch testing; measures of control must rather be in the nature of job transfer, cleanliness and skin-protective devices. Burns produced by the action of strong acids and alkalis can usually be prevented by proper work methods and protective clothing. Prevention of the defatting effects of strong solvents, with drying, fissuring and dermatitis, lies mainly in the use of mechanical aids in manufacturing, in protective clothing and in the restoration of the fat content of the skin.

Dermatitis due to chlorinated naphthalenes and diphenyls, waxes used in the insulation of electrical cables, is most troublesome in the installation of these cables in fighting ships. Control is effective only through proper hygienic methods. A cleansing mixture of butyl stearate and sulfonated castor oil, which removes the wax from the skin, has been suggested and seems effective.⁵¹

Anthrax, an infection entering usually through the skin, is still of frequent occurrence, cases continuing to be noted among wool sorters, tannery workers and others engaged in the transport of these materials. Control lies in prompt attention to minute abrasions in workers potentially exposed to this hazard, of which it is essential that they be made aware. Methods of treatment, including serum and sulfonamides, are effective if promptly applied. Penicillin has been reported to be effective in 1 case.⁵²

PUBLIC-HEALTH ASPECTS

Industrial hygiene includes in its scope numerous activities related to the general health of the

worker. These have quite rightly come to the fore in the wartime program, since it is recognized that specific occupational disease accounts for no more than 5 per cent of the workers' disability from illness and that the general sicknesses to which mankind is heir account for the rest. Hence, in keeping the worker on the job, it is most important to attack directly all problems that affect morbidity and mortality, including those due to a hazardous working environment.

In many states a program of tuberculosis case finding in industry has been undertaken by means of a mass survey. This has been aided by the development of a photofluorographic unit, a number of which have been placed at the disposal of state industrial-hygiene divisions by the United States Public Health Service.⁵³ A venereal-disease program has been outlined and is gradually making progress, although it is less readily accepted by industry than are some other public-health measures.^{54, 55} Problems of sanitation and community health that affect the industrial environment have also received attention.

Probably the most significant advances have been those in the field of nutrition, and numerous developments have brought attention to this phase of public health so important to the worker. The special problems of in-plant feeding, outfeeding, nutritional requirements, food costs, vitamin supplements and so forth have been integrated into programs that are finding widespread acceptance in industry.⁵⁶⁻⁵⁸

Although hampered by the paucity of physicians, nurses and equipment available, many industries have adopted pre-employment and periodic examinations and have established medical departments with adequate equipment and staff. Developments are under way in the provision of medical and nursing care to small industries through visiting nurses' associations and other agencies.

The great influx of women into the nation's factories has caused their place in industry to be carefully studied by the United States Department of Labor, the United States Public Health Service and the state industrial-hygiene units. Standards have been promulgated for the effective employment of women, taking into account their physical characteristics.⁵⁹

Education in industrial health has by no means been neglected, and an active program is being formulated by the United States Public Health Service. The problem of absenteeism and its causes has received careful analysis, and progress has been made toward reducing this defect in the all-out war effort.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 29521

PRESENTATION OF CASE

A sixty-nine-year-old retired schoolteacher was admitted to the hospital because of pain in the epigastrium and left shoulder of three hours' duration.

The patient was in excellent health until ten or twelve years before admission, at which time she began to have epigastric distress without any real pain. The distress was described as "acidity." She had occasional gaseous eructations but no vomiting. She was given a Sippy powder after each meal, which relieved the burning. She had continued to take the powder.

Ten years before entry she had a "typical story of coronary thrombosis for which she was given bed rest and morphine." Eight years prior to admission she became a vegetarian. There was a 20 or 30 pound loss in weight following this. The epigastric distress continued and was relieved by the Sippy powder.

Two or three weeks before entry, there was increase in the severity of the symptoms and for the first time she developed epigastric pain, which increased on the day of admission. After taking the Sippy powder, she suddenly became extremely sick and vomited "brownish, bloody material." The pain disappeared but she remained weak. She had noodles for supper, following which she became nauseated, went to the bathroom and fell down unconscious, striking her forehead. There was no vomiting or bowel movement at that time. It was not known how long she remained unconscious. On becoming conscious she vomited brownish material followed by bright-red blood. "Later" she had a black tarry bowel movement. Either before the vomiting or after it, she complained of burning epigastric pain, which radiated to the back and to the left shoulder and was accompanied by marked dyspnea. Morphine, administered by her physician, relieved the pain.

Physical examination on admission showed a

thin, acutely ill woman sitting up in bed. She was cyanotic and breathed in a rapid, shallow manner. She had periods of drowsiness, but between these she was fairly alert. There was slight dullness over the right base; the breath sounds were normal, and there were no rales. The heart was enlarged to the left. The sounds were of fair quality, and a soft apical systolic murmur was heard. The abdomen was distended, tympanitic and "firm," but there was no spasm, tenderness or masses. Peristalsis was normal. Pelvic and rectal examinations were negative.

The blood pressure was 154 systolic, 80 diastolic, on the right, and 130 systolic, 70 diastolic, on the left. The temperature was 99°F., the pulse 90, and the respirations 38.

Examination of the blood showed a red-cell count of 4,000,000, with 13.7 gm. of hemoglobin. The white-cell count was 16,000, with 97 per cent neutrophils. The urine was normal, with a specific gravity of 1.022. The stools were tarry, with a ++++ guaiac test.

X-ray examination showed no definite air below the diaphragm. There was a peculiar shadow behind the heart, which could represent air within the mediastinum or disease within the lung. A repeat x-ray examination on the following day showed areas of atelectasis at both bases and probably a moderate amount of fluid in the left pleural cavity. Films of the abdomen showed considerable gas and fecal material in the colon but no definite evidence of intestinal obstruction. During the course of examination she had an episode of "bradycardia with arrhythmia" associated with fainting. This lasted one or two minutes and did not recur. She continued to vomit dark-brown, guaiac-positive material for the next two days. The pain persisted and was worse with respiration. She was given intravenous fluids.

On the third hospital day the temperature rose to 104°F., and the pulse to 140, but the respirations remained around 40. Examination showed dullness over the left chest from the fifth interspace down posteriorly, with diminished breath sounds, tactile fremitus and vocal fremitus. Grocco's triangle was present, as was an area of bronchial breathing at the right base near the spine. There was a questionable friction rub in the left axilla. X-ray examination of the chest revealed a considerable amount of fluid in the left pleural cavity. A swallow of barium showed a large diverticulum in the lower esophagus. No free air could be seen under the diaphragm. The stomach contained a considerable amount of fluid, and the single swallow of barium dropped through the retained fluid and food. Examination was discontinued. A chest tap yielded 200 cc. of blood-

*On leave of absence

tinged, nonodorless fluid, which showed 1500 red cells and 5000 white cells per cubic millimeter, with 90 per cent polymorphonuclears and 10 per cent lymphocytes. A culture of the fluid showed many colonies of nonhemolytic streptococci and few of colon bacilli. The patient was given 5 gm. of sodium sulfadiazine. The following day she was distended and had some tenderness but no spasm. Another 350 cc. of fluid was withdrawn through a tap in the ninth interspace, without any improvement in the dyspnea. The fluid was brownish, cloudy and foul smelling.

The temperature slowly fell, but the pulse and respirations remained more or less stationary. The blood pressure was 140 systolic, 85 diastolic, in both arms. Despite oxygen therapy, the patient became steadily more cyanotic and died on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM B. BREED: I do not believe that this woman had coronary occlusion at any time. I believe that she had some congenital defect in the diaphragm. She may have had an ulcer in or about a hiatus hernia. Certainly she had some gastritis in that area, which would explain a good deal of the story later on. I think that there was a rupture of some part of the gastrointestinal tract into the left pleural cavity. Just where it was—in the stomach or in the colon—I do not as yet know. Let us go through the data and see how firmly such a diagnosis stands.

The "acidity"—a symptom that might have responded well to Sippy powders—could perfectly well have been due to a small hiatus hernia or gastritis. Regarding the story of coronary thrombosis, let it be remembered that symptoms due to hiatus hernia are often confused with those of coronary heart disease; and we have no evidence, except the patient's own statement, that she ever had a coronary occlusion. The disease process that I have already mentioned could perfectly well have produced the symptoms described. We have no evidence at hand that she had a bad heart, and no electrocardiogram to indicate old scarring or recent coronary disease. The heart sounds were said to have been good, and the heart was said to have been enlarged to the left. Too much emphasis should not be placed on this clinical observation in the presence of disease in the left pleural cavity. Two or three weeks before she came in she certainly had gastrointestinal bleeding, which could have been caused by a hiatus or diaphragmatic hernia, or by an ulcer in that region. Ulcers occasionally do occur in the region of a hiatus hernia. We know that gastritis may be present about a diaphragmatic hernia, and that a patient may bleed from either of these conditions. I

have never personally known or read of a case in which a hiatus hernia perforated into the pleural cavity. I am presupposing that she had a defect in the diaphragm. I do not know how much of the gastrointestinal tract might have herniated through from time to time. There may have been a perforation, let us say, of the colon. We know that the stomach does not contain colon bacilli. We know that there were a few colon bacilli found in the left pleural cavity along with nonhemolytic streptococci. She had no evidence of chronic anemia or of blood loss. She had some leukocytosis, which could be explained by an infectious process in the left pleural cavity. She had occult blood in the stool two or three days after the initial hemorrhage, which does not necessarily mean she was still bleeding.

I should like to ask a few questions about the x-ray examination. In two places it is stated that no definite air was seen below the diaphragm. I should like to have comment on that. I should also like to have explained the statement: "The stomach contained a considerable amount of fluid, and the single swallow of barium dropped through the retained fluid and food. Examination was discontinued."

DR. LAURENCE L. ROBBINS: I do not know why it was discontinued unless the patient's condition was poor. Probably the reason why the statement about no free air beneath the diaphragm was made is that there was a question of perforated hollow viscus. I am not at all sure that the films were taken in the correct position to determine whether there was free air beneath the diaphragm. Assuming that they were, there is no visible free air. There is a process in the left lower lung field that apparently consists of fluid within the pleural cavity; this markedly increased in amount in twenty-four hours. There probably is consolidation in the left lower lobe. One shadow definitely bothers me, and that could be a hernia.

DR. BREED: It could be part of the stomach?

DR. ROBBINS: Yes; but I am not sure that it is. I do not know what the fluoroscopist thought. His examination was probably not sufficient to rule out a hernia. The diverticulum that was described is this dense shadow just below the bifurcation of the trachea, and again we have to take the fluoroscopist's word that it is a diverticulum, which is most likely. We have evidence of a large amount of fluid and other material in the stomach.

DR. BREED: What about the swallow that dropped down through the fluid? Either it means something or it should not have been put in.

DR. ROBBINS: It is merely an indication that there was foreign material in the stomach and

that the patient was not adequately prepared for a gastric examination.

DR. BREED: Certainly you see no barium above the diaphragm in either of these films.

DR. ROBBINS: No.

DR. BREED: You speak of a ruptured viscus. Are you thinking about stomach, esophagus or colon—the same things I have mentioned?

DR. ROBBINS: Yes.

DR. BREED: You would not like to add anything more?

DR. ROBBINS: No. I do not believe that the x-ray examination was complete.

DR. BREED: I take it that on the first examination the left chest was clear, since it is not mentioned in the record. Perhaps Dr. Beckman knows about this case. Do you?

DR. WILLIAM BECKMAN: Yes.

DR. BREED: Then there was quite a sudden change in the examination of the left chest?

DR. BECKMAN: Yes.

DR. BREED: That is very striking and certainly leads one to suspect that the foul-smelling fluid that was removed after twenty-four hours contained more colon bacilli than did the fluid obtained at the original tap. If so, then one would certainly look below the pylorus for the source of this fluid. As I have already mentioned, the normal stomach is peculiarly free from colon bacilli, nor does the duodenum contain many colon bacilli. If we could be assured that the foul-smelling odor of this fluid was due to the colon bacillus, we should have to assume that it was coming from the large or small intestine. Of course the patient may have had vascular disease, but I am inclined to doubt it. One must always consider such a condition with a sudden change in the chest, especially in view of the fainting spell during the x-ray examination. I can get nothing from the x-ray examination, however, that makes me change my initial impression from reading the case over. I still believe that there was a rupture of some portion of the gastrointestinal tract, presumably below the pylorus, into the pleural cavity through a congenital lesion in the diaphragm. Whether the patient also had an ulcer, I do not know. There is no evidence one way or the other.

I am doubtful about the coronary thrombosis and I do not believe that evidence of an old coronary occlusion was found. The patient presumably died of sepsis in the pleural cavity—a rather unusual type of empyema—and possibly cardiac collapse, which was not due, however, to any specific heart disease.

DR. HELEN PITTMAN: If there was rupture of a hollow viscus into the pleural cavity, how about air in the pleural cavity? The x-ray films do not appear to show such a finding.

DR. ROBBINS: Air is not necessarily present. For example, a perforation of a peptic ulcer of the esophagus shows little air in the pleural cavity.

DR. BREED: I am not interested in the diverticulum of the esophagus. I should like to add that I do not believe the patient had cancer of the stomach or of the lower end of the esophagus.

DR. MARIAN ROPES: We were impressed with the story of ulcer symptoms for the ten years before entry and did think at first that the hemorrhage came from the ulcer and that the ulcer had perforated into the abdomen. But it soon became apparent that that was not true. We did not properly connect the findings in the left pleural cavity with the process in the gastrointestinal tract.

CLINICAL DIAGNOSES

Bleeding peptic ulcer.

Empyema, left.

Coronary thrombosis, old.

DR. BREED'S DIAGNOSES

Empyema, due to perforation of gastrointestinal tract (presumably below the pylorus).

Diaphragmatic hernia.

ANATOMICAL DIAGNOSES

Peptic ulcer of esophagus, with perforation into left pleural cavity.

Empyema, left.

Myocardial infarct, old.

Diverticulosis of duodenum, jejunum and sigmoid.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy showed an empyema in the left pleural cavity composed of 600 cc. of turbid, somewhat hemorrhagic fluid. The abdomen was negative. We were unable to find anything in the stomach or duodenum to account for the long-standing ulcer symptoms. At first we were at a loss to explain the cause of the empyema; then Dr. Sniffen found a good-sized hole at the lower end of the esophagus. There was a peptic ulcer of the lower end of the esophagus that accounted for the long-standing ulcer symptoms and had perforated into the left pleural cavity. In the mediastinum was an abscess 3 or 4 cm. in diameter.

The patient had evidence of old coronary thrombosis. The left descending branch of the coronary artery was completely occluded, and we found an anterior healed myocardial infarct.

DR. BREED: The diaphragm was intact?

DR. CASTLEMAN: Yes.

DR. ROBBINS: There was no hiatus hernia? Is it not rather rare to find peptic ulcer of the esophagus without hiatus hernia?

DR. CASTLEMAN: I do not know. It is rather difficult at autopsy to be sure of a slight hiatus hernia. If one did exist, it would probably have been reduced at the time of autopsy.

CASE 29522

PRESENTATION OF CASE

A seventy-three-year-old retired lawyer was admitted to the hospital because of weakness and tiredness.

The patient was in good health until about six months before entry, when, while working in his garden, he felt unusually tired and weak. He continued his activities, but at a slower pace, until eight weeks prior to admission, when he felt extremely weak and went to bed, where he stayed except for a daily trip to the bathroom. He had no fever, chills, night sweats or headaches. In the following four weeks he noticed a sore spot near the tip of the sternum on swallowing. At times there was a sensation of pressure on the chest and an occasional dry cough. His appetite became poor but his bowel movements remained the same as before. One month prior to admission, examination by his family physician was entirely negative except for a small right indirect inguinal hernia. The temperature was 101°F., the pulse 100, and the blood pressure 140 systolic, 70 diastolic. The urine was acid, with the slightest possible trace of albumin. The sediment contained a few white cells but no red cells. The hemoglobin was 60 per cent. The patient was placed on sulfadiazine, 1 gm. four times a day. Two days later the family physician thought that there were possible rales at the left base and an enlarged spleen. The temperature was 99.4°F. In the next two days the cough completely disappeared, the temperature became normal, and the pulse was 96. He had received 40 gm. of sulfadiazine, which was then discontinued. He was placed on iron and vitamin B tablets but refused to take them or to see his physician. He remained in bed. The substernal pain persisted. It was described as a steady, nonradiating pain that felt like "fifteen men on a dead man's chest"; it was not relieved by food or change of position but sometimes went away spontaneously. The patient refused all solid foods although he said that they caused no discomfort. A friend, however, stated that "solid foods seemed to catch on the way down." The patient subsisted on liquids and semisolids, taking them at odd hours instead of the usual mealtimes. There was occasional nausea but no vomiting, hematemesis, bloody or tarry stools and no numbness or tingling of the extremi-

ties. Two days before admission he developed a fever of 102°F. The next day his physician noticed marked pallor and weight loss since the last visit.

Physical examination on admission showed a well developed, rather emaciated, extremely pale man in no distress. The skin was pale and dry; the tongue was normal. The mucosa of the posterior part of his mouth was covered in areas by patches of white exudate with no surrounding inflammatory reaction. The teeth were in poor condition. The pharynx was covered with a thin mucinous discharge. The heart and lungs were normal. There was a small right inguinal hernia. Vibration sense was diminished in the legs, but neurologic examination was otherwise normal.

The blood pressure was 126 systolic, 56 diastolic. The temperature was 101.2°F., the pulse 118, and the respirations 24.

Examination of the blood showed a red-cell count of 980,000, with a hemoglobin of 3 gm. per cent. The white cell count was 1400. Only 86 cells could be seen in the smear. Of these 22 were neutrophils, 28 large lymphocytes, 16 small lymphocytes and 20 monocytes. The red cells were large and well stained. There was some anisocytosis. No reticulocytes were seen. The urine had a pH of 5.5 and a specific gravity of 1.016. There was a + test for albumin. One or two white cells were seen in the sediment. The stools were guaiac negative. A blood Hinton test was negative. The hematocrit was 13 per cent. The mean corpuscular volume was 133 cubic microns, the mean corpuscular hemoglobin 31 micromicrograms, and the mean corpuscular hemoglobin concentration 23 per cent. The nonprotein nitrogen was 23 mg. per 100 cc. Gastric analysis showed no free acid and a combined acidity of 8 units. At the end of thirty minutes the free acid was 5, and the combined acid 25.

X-ray films of the chest showed no definite evidence of consolidation or shift of the mediastinum. A gastrointestinal series revealed no definite abnormality of the esophagus or stomach. There were at least three large diverticula of the second and third portions of the duodenum. The duodenal cap showed a pressure defect on the superior surface, which was interpreted as being probably of no clinical significance.

From the time of admission the patient had a persistent fever, the rectal temperature reaching 102°F. daily. During this period he coughed continually but raised no sputum. He was placed on iron and liver, without response. On the third hospital day he had two severe shaking chills. The temperature spiked to 103°F., and the respirations rose to 30. There was no chest pain or increased

cough. Examination showed dullness, bronchial breathing, increased spoken and whispered voice, and rales over the left lower lung field. The white-cell count was 700, but no white cells could be found in the smear. He was given intravenously 4 gm. of sulfadiazine in 1000 cc. of 5 per cent dextrose in water and 500 cc. of whole blood. He remained alert. The temperature gradually rose to 104°F., and he died on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. JOHN W. NORCROSS*: This patient was a seventy-three-year-old man with progressive anemia, leukopenia and intermittent chest pain of about six months' duration. Before going into a detailed differential I should like to consider a few points in the history.

The initial complaints were fatigue and tiredness, which of course could have been entirely due, and probably were, to the anemia. The patient also complained of pressure on his chest. Any man with severe anemia, particularly a man of seventy-three, is entitled to angina pectoris, and I think that this must be considered as a possible cause of the pain that he had in the chest. But it was not typical angina, since, as later described, it was nonradiating and steady; angina at times, however, can be almost constant. I also want to point out that the patient had a small amount of albuminuria. So far as we know from the history, the hemoglobin was 60 per cent before he received sulfadiazine. Furthermore, the family doctor thought that the spleen was enlarged, but nowhere else is there any mention of this, and we have to assume that numerous physical examinations made on this man after he entered the hospital did not show a palpable spleen. There are many negative factors mentioned later in the history that are of importance. There was no vomiting, hematemesis, bloody or tarry stools or paresthesias. When he entered the hospital there was no distress, emphasizing the intermittency of the chest pain. The note is made that the vibration sense was diminished. We are not told how much, but we must remember that in a man of seventy-three, owing to the probable presence of arteriosclerosis, this observation is of little clinical importance. The fact that no lymph nodes were felt may be significant. The laboratory notes show that he had a severe macrocytic, hypochromic anemia. Later I shall say more about the blood smear, which Dr. Castleman kindly let me have. The patient had free acid in his gastric analysis. I assume that the test meal was used in doing this analysis, since if histamine had been given there probably would have been more than 5

units of free acid present. At any rate he did not have achlorhydria.

I should now like to see the x-ray film of the chest.

DR. GEORGE W. HOLMES: I do not see anything definitely wrong in the chest.

DR. NORCROSS: Can you see anything in the bones that might be abnormal?

DR. HOLMES: No. The shadow of the right auricle is possibly a little prominent, but it is well within normal limits. For a man of his age he shows surprisingly little evidence of arteriosclerosis. There is no tortuosity of the aorta, and no visible calcification in the wall. The vessels around the root of the lung are large, but perhaps these are of no great importance. These films show some barium in the esophagus, but we shall have to take the word of the man who did the fluoroscopy that there were no varices. I cannot rule them out from this one film. Diverticulums are scattered along the duodenal loop, but unless there was some question of disease in the pancreas, I should not think they had any particular bearing on the case. The distance between the duodenal loop and the diaphragm is rather short, and one might expect the liver to be small rather than large, although that is not a definite finding.

DR. NORCROSS: On the film showing the spine do you see anything to make you worry about the bones?

DR. HOLMES: No.

DR. NORCROSS: The patient had a persistent fever, cough and apparently a terminal pneumonia. With regard to a detailed differential diagnosis, one condition that must be considered in any man of this age is an overwhelming infection, which can cause the blood picture given in the abstract. Miliary tuberculosis likewise can do this. In addition, a worn-out bone marrow could lead to an anemia and leukopenia of this degree. Although it is not so stated in the history, the smear showed a normal number of platelets, an observation that is against a diagnosis of bone-marrow depletion. The duration of six months is also against it. We might even consider the possibility that one of the diverticulums ruptured and caused a localized peritonitis. In a man of this age the signs as well as the symptoms may be extremely confusing and such a patient can have an abscess in the abdomen without much to show for it on physical examination. Here again, I think that this is extremely unlikely, but should be put into a differential diagnosis. Blood loss either extrinsic into the bowel or intrinsic in the form of a hemolytic process seems unlikely. Blood loss would not account for the extreme leukopenia, and there is ample evidence that the patient did

*Physician, Lahey Clinic

not lose blood from the gastrointestinal tract. From a hemolytic point of view, particularly a hemolytic process coming from a drug or toxic chemical of one kind or another, we should have to assume that he had agranulocytosis in addition to a hemolytic anemia to account for this blood picture. Of course hemolysis leading to such a severe anemia would be accompanied by jaundice, which would be visible to the examiner. This apparently was not the case.

Severe pernicious anemia must be considered. The vibratory change is not significant, but it is important that free hydrochloric acid was demonstrated in the gastric analysis. In my opinion, true pernicious anemia does not have even this amount of free acid in the gastric contents. Furthermore, there was no response to liver therapy. I do not know over how long a period he received liver, but he was in the hospital for five days and at least in that time he did not respond, which is strongly against pernicious anemia. Furthermore, the platelets were normal in the smear and certain other changes in the blood were not characteristic of pernicious anemia.

Carcinoma with metastases is a possibility. We do know that one can have widespread metastases in the bone that do not show by x-ray examination. The type of chest pain could come from metastatic disease in the spine, sternum or ribs. The type of change in the blood, however, is usually different, there usually being more of a myeloid, leukemoid picture, which was not present in this case. Agranulocytosis of course does not explain the anemia. Aplastic anemia, or more correctly hypoplastic anemia, does not explain it, because in this disease the platelets are of necessity reduced along with the other elements. Leukemia, lymphoma and Hodgkin's disease could cause this picture, but again we have no evidence of enlarged spleen, liver or nodes, and with what evidence we have, one would have to be brave to make any one of these diagnoses.

There is one condition that I think is more likely—namely, multiple myeloma with widespread bone-marrow involvement that was not sufficiently localized in any one place to show by x-ray study. The type of pain from which he suffered may be said to be characteristic of, or at least completely compatible with, this diagnosis. The remissions of the pain are also typical. Usually patients with multiple myeloma do not have much change in the platelets and may on occasion have just as severe an anemia and leukopenia. The latter is unusual, of course, but this is an unusual case.

In connection with this point, I should like to make some comments on the smear. I might say that I do not agree entirely with the differential given in the history. According to my interpretation, there were 37 per cent neutrophilic cells, 1 per cent being myelocytes. Most of these cells were perfectly satisfactory neutrophils. Forty-eight per cent were lymphocytes, of which only 5 per cent were normal, all the rest being atypical in one or more ways. In addition to these lymphocytes, 12 per cent were characteristic of cells found in patients suffering from multiple myeloma, 2 per cent being typical plasma cells, and 10 per cent so-called "myeloma cells." There were also 3 per cent blast forms. In addition there was rouleaux formation. I do not want to say too much about this, as it was not outstanding, but in areas of the smear that were thin and would not ordinarily have rouleaux formation there was a considerable amount of it.

The weakness, fatigue and various other things are amply explained by this diagnosis. The patient did not have much albumin in the urine. We do not know whether Bence-Jones protein was present. There are many patients with myeloma, however, who have no more albumin than this, and this albumin may have been Bence-Jones protein. The absence of palpable lymph nodes and enlarged spleen is perfectly characteristic. I should obviously like to see some x-ray evidence to help me here, but I do not believe that the lack of it rules out the diagnosis. I should also like to know about the total protein and the sedimentation rate, as well as the findings of a bone marrow biopsy, but I assume they were not done. I believe that this case can fit in with the diagnosis of multiple myeloma, with terminal bronchopneumonia.

DR. WILLIAM A. BISHOP: I was much puzzled when I was called to see this patient outside the hospital. I obtained a sketchy and not too reliable history. He had a fever, and although I could not find anything definite in the lungs, I went on the hunch that he must have had an upper respiratory infection. The cough was considerably worse than is stated in the record, although it was unproductive. On that basis, I gave him sulfadiazine. He was a peculiar type of person, who really did not want to see me, and I was called only because the people in the house were anxious about him. So I met an unresponsive, resistant patient from whom it was difficult to get a good history. But, as stated in the record, he had had a definite six-month period of feeling tired. When I first saw him he was pale, but not so markedly

as when he entered the hospital. I saw him three times and was told not to come again. They had no telephone, but I finally got a message to him telling him to stop taking the sulfadiazine and to begin the iron, liver and vitamins. Since the temperature had fallen to normal on the third day,

cough at that time, and of course the severe anoxia was evident.

DR. BENJAMIN CASTLEMAN: Dr. Beckman would you like to tell us about your impression?

DR. WILLIAM BECKMAN: I did not have much to say of this patient. I saw him once with the med-

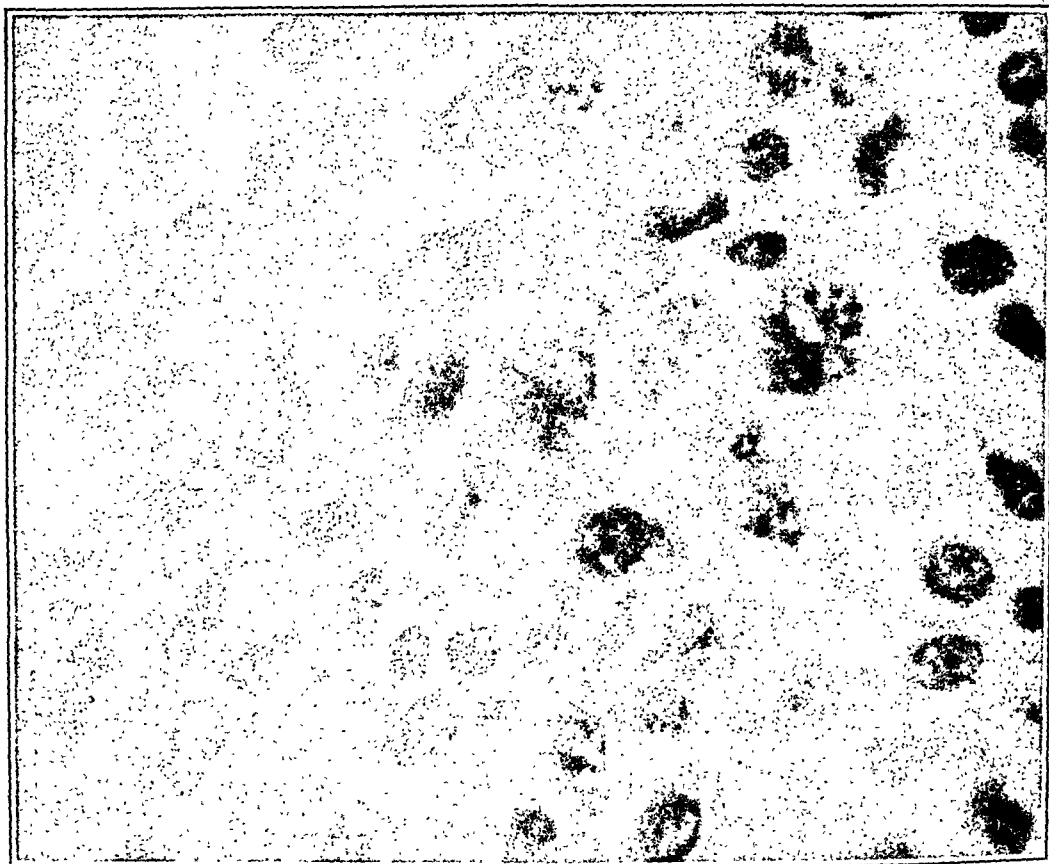


FIGURE 1. *Photomicrograph of the Wall of the Esophagus Showing Plasma-Cell Infiltration.*

I thought that only a day or two more of the sulfonamides was necessary. The thing that he chiefly complained of was pain, or the pressure, as he called it, of "fifteen men on a dead man's chest," at the lower end of the sternum. I do not believe that this was angina, since the pain did not radiate. Then I was struck by the fact that it was painful for him to swallow, and entertained the thought that there might have been something in the esophagus. That was about the picture when I left him, and I was frankly quite at sea. Eight days later I was again called. The temperature was 102°F.; the patient looked worse, being much paler, and had lost weight, with the story that he had continued to refuse food except liquids. He also refused medicine, saying that it hurt him to take it. I thought that I could hear something in the lung bases and sent him to the hospital on the following day with a diagnosis of probable bronchopneumonia. He had fever and

students, and I must say that I did not even come close to the diagnosis. I thought that he had aplastic anemia and suggested giving liver in capsules. It was atypical pernicious anemia, with the hope that he might get a response before he succumbed to the obvious pulmonary sepsis that he had at the time.

CLINICAL DIAGNOSES

Aplastic anemia.
Lobar pneumonia: left lower lobe.
Generalized arteriosclerosis.

DR. NORCROSS'S DIAGNOSES

Multiple myeloma.
Terminal bronchopneumonia.

ANATOMICAL DIAGNOSIS

Plasma-cell leukemia, with involvement of liver, marrow, spleen, lymph nodes, esophagus, lungs and kidneys.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The autopsy on this man showed an unusual esophagus. Practically the whole esophageal wall, from the beginning to the cardia, was markedly thickened, measuring in places 4 to 5 mm., and was rigid, as if there were submucosal infiltration. It had a dirty, brown-black appearance. On gross examination we were unable to decide what it was. It certainly did not look like carcinoma of the esophagus, and there was no ulceration of the mucosa. The liver was about normal in size, and the spleen slightly enlarged, weighing 290 gm., but neither presented any gross abnormality. The kidneys were slightly enlarged and pale, which one might expect with anemia.

Microscopical examination, however, told the whole story. A section through the wall of the esophagus showed the infiltration that we were able to see in the gross. Practically all the cells were characteristic atypical plasma cells (Fig. 1). In one lymph node, a peripheral sinus was completely filled with plasma cells. Sections of the bone marrow and spleen, as well as those of the lungs and kidney, also showed numerous plasma cells. There were no isolated foci of myelomatous infiltration in the bones, the lesions being diffuse, which, as Dr. Norcross has stated, makes them difficult, if not impossible, to see in x-ray films. We were unable to find any myeloma casts in the tubules of the kidney.

I believe that the case should be classified as plasma-cell leukemia, with diffuse infiltration of the lungs, liver, spleen, kidneys and lymph nodes, as well as the bone marrow, rather than multiple

myeloma. Of course the two diseases are the same, but in the leukemic type the plasma cells get out into the peripheral blood in larger numbers than they do in the average case of multiple myeloma. Looking back in our records we found two similar cases—in men sixty-four and sixty-five years old respectively. One had a red-cell count of 1,500,000, and the other a count of 700,000; one had a white-cell count of 1500, and the other a count of 1200. These patients also complained of fatigue and were clinically diagnosed as having aplastic anemia.

DR. HOLMES: Are there any other cases with this type of esophagus?

DR. CASTLEMAN: I cannot recall one, but any kind of leukemia may produce this type of infiltration. Certainly the substernal pain was caused by the esophageal disease.

DR. HOLMES: Under the fluoroscopic examination, the esophagus should have failed to dilate when the patient swallowed. It ought to have been possible to see that the esophagus was rigid. From these films, however, I get the impression that this man was in poor condition and that the examination was incomplete.

DR. JOSEPH AUB: Abnormal white cells are more susceptible to sulfonamides than are normal cells. Livingston,* at the Huntington Memorial Hospital, showed that sulfonamides drop the white cell count enormously in leukemia.

DR. CASTLEMAN: You think that that might also apply to plasma cells?

DR. AUB: I wonder if it would.

*Livingston, K. E., and Moore, R. D. The reaction of leukemia patients to sulfapyridine administration. *New Eng J Med* 223:975-983, 1940

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1944—A YEAR OF DECISION

THE year on which we are embarking may well be a year of decision for this generation and for generations to come. With almost no decision on our part we have been forced into a test of power, limitless in its geographic scope; this year, if we are true to our destiny, we shall achieve the first of our final victories. The costs of this victory, and its dangers, are yet to be computed; but whether we shall come through it with a clear future or a confused and clouded one is a decision that soon must be made.

It has become a truism that we can win the war and lose the victory, as we lost it in 1918 and 1919 and in the twenty-odd years thereafter. We are also told that we are fighting and work-

ing and paying to preserve our old way and yet we know that many of the foundations of that way of life are not worth preserving. There is anything in this war that is worning, besides security, it is a new way of life, a better way of life for all of human kind. We are not ashamed to say that spiritual and intellectual values must be reckoned ahead of material ones.

To many Americans, still, the idea of progress suggests plenty of gasoline, endless rubb roads, and development of the plastics industry to keep pace with the new magic of electronics. These developments will probably be given peace and prosperity, but there has been a certain fiscal association with the word progress in our past history, that limits its meaning in a rather unfortunate manner.

The real problems that are going to make a year of decision are those that can be solved only by clear-sighted planning and fact-finding. We are going to begin to be confronted with the necessity of a switch-back of industry to a peacetime basis, with a major unemployment problem. We are going to meet the vanguard of seven million young men, crippled and well, who will have to see the rewards of the victory they have won. We are going to decide whether we can continue to play ball with our allies, once the immediate danger is past, or whether we are going to scramble for the major part of the fruits of the victory—to see who can dominate the air routes, shipping lanes and the richest markets. We are going to see if we can play a mature role in international politics and world statesmanship, after the terms that we have professed—protecting and patronizing, helping without bullying and operating without assuming a leadership that has not been earned. This may be the year when we shall have to decide whether, as a nation, we have become of age—if we are mature enough to be granted a leadership in settling the most perplexing problems with which the world has ever been confronted.

FATIGUE LABORATORY

Fatigue Laboratory of the Harvard School of Business Administration was the result, more directly, of the wisdom and foresight of Wallace B. Donham who, during his term of office, appreciated the possibilities of research under the conditions with which industry is confronted. The laboratory was accordingly set up, in 1918, under the auspices of the Rockefeller Foundation, and continues to function with the aid of the National Research Council.

Late Professor Lawrence J. Henderson directed the establishment of the laboratory and his wisest counsellor, under the successive directorships of Dr. Arlie V. Bock and Dr. D. B. Dill, Lieutenant Colonel Dill continues his interest during the present activities of the laboratory. The active directorship has passed back into the hands of Dr. Bock for the duration of the war, with the practical functioning of the laboratory in the hands of Drs. R. C. Darling, J. P. Fortes and Robert E. Johnson.

Except for a small flame of pure research that is burning at the laboratory until better days of academic pursuits have returned, the work being conducted is done entirely for the purpose of Scientific Research and Development and for the Quartermaster Corps of the Army. Thus, in a cold room, with a minimum temperature of 50°F., various types of warm clothing, including electrically heated suits and shoes, are worn on the living subject; here also, stiffly resistant, lies "Oscar," the electric dummy, within whose patient frame is measured the amount of heat required to keep his body temperature up to human normal with the aid of various styles and types of garments. In another chamber, temperature and humidity are attained, and here, experiments are conducted on heat exhaustion, acclimatization, and the best types of clothing for use in climatic conditions, with a three-and-a-half-day-an-hour march simulated on an electric treadmill. Still another chamber furnishes the barometric pressures of various altitudes.

Nutrition studies based on the standard field rations are being conducted, with a view to their balance, particularly regarding the vitamin B fractions; studies have been made under field working conditions on the protein requirements of the body, and it has been found that good health and nutrition can be maintained on a protein intake considerably below the traditionally accepted 70 gm. per day, with those that are provided being principally from vegetable sources.

In addition to its homework, the laboratory is constantly on call to send its investigators into the field wherever needed, to make their studies under actual living and working conditions. Its official reports run into volumes, and when, finally, the veil of secrecy can be lifted, it will be found that scientific progress has taken some tremendous steps in various directions during the war years.

Indefinite and inclusive as the term "fatigue" may be, the Fatigue Laboratory has long since outgrown its title.

MEDICAL EPONYM

PANDY REACTION

The paper "Über eine neue Eiweissprobe für die Cerebrospinalflüssigkeit [A New Albumin Test for the Cerebrospinal Fluid]" by Kalman Pandy (b. 1868) appears in the *Neurologisches Centralblatt* (29: 915-919, 1910). A portion of the translation follows:

This test consists in adding a drop of cerebrospinal fluid to about 1 cc. of concentrated carbolic acid (1 part carbolic acid crystals plus 15 parts of distilled water). Wherever the two fluids come in mutual contact there appears after a few seconds a bluish white turbidity resembling a cloud of smoke—an indication that in the fluid in question there are easily precipitable proteins (globulins) in pathological quantity.

R. W. B

CORRESPONDENCE

A WARTIME EMERGENCY DIABETIC COMA SERVICE

To the Editor: Early diagnosis and treatment of diabetic coma lessen mortality and hasten recovery. With this in mind, the Coma Service has been organized at the Massachusetts General Hospital.

Through the co-operation of the hospital, a corps of diabetic nurses, a chemical technician and the medical staff, blood and urine analyses, as well as medical treatment and special nursing, will always be available, day and night, Sundays and holidays. Such a service would be desirable for all hospitals, but unfortunately on account of war conditions this is not feasible.

Any doctor who has a case of diabetic coma in or outside a hospital and cannot secure the laboratory and medical assistance that he believes indicated can feel at liberty to call on the Emergency Diabetic Coma Service at the New England Deaconess Hospital for consultation regarding treatment or admission of the patient.

WARREN F. COOK
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DEPRIVATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held November 19, the Board voted to revoke the license to practice medicine in this Commonwealth of Dr. Aaron O. Bernstein, 634 Page Boulevard, Springfield, and formerly of Gardner and Winchendon, because of gross professional misconduct in the practice of his profession.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

BOOK REVIEWS

Biological Symposia. Edited by Jaques Cattell. Volume VIII. *Levels of Integration in Biological and Social Systems.* Edited by Robert Redfield. 4°, cloth, 240 pp. Lancaster, Pennsylvania: The Jaques Cattell Press, 1942. \$2.50.

The contributions to this interesting volume represent new frontiers of research for students of human society. The papers are all concerned with one or another aspect of the question, How are parts constituted into wholes throughout the range of life-forms?

An informative and critical introduction is written by Robert Redfield. Libbie H. Hyman, in "The Transition from the Unicellular to the Multicellular Individual," points out that the essential difference between a protozoan colony and a multicellular individual is polarization, the establishment of an axis along which there is both functional and morphological differentiation. "Intermediate Levels of Organismic Integration," by J. William Buchanan, sums up his position in the declaration that the organization of animals of the lower groups is characterized by an absence of centralization of the response mechanisms. In the chapter "Higher Levels of Integration" R. W. Gerard notes that the difference between lower and higher organisms is mainly in their transmissive mechanisms and in their adaptive amplification. Man as an org is selfish, individualistic and dominated by the old brain and its emotional attributes.

Man as a unit in the epiorganism is altruistic and operative, and depends on the functioning of his brain and its intellectual attributes. William Burrows, his paper "Synergistic Aspects of Bacterial Population," questions the validity of the concept that specific microetiology is the basis of much of modern bacteriology and suggests that diseases may be caused not by a single species of bacterium but by associated micro-organisms. H. S. Jennings concludes that the transition from the individual to the social level begins in the one-cell organisms; and advances there by several steps. Thomas Parsons considers the problem of integration in infrasocial insect populations, with marked emphasis on the argument that population is as much a biologic unit as the organism and has the attributes of preproduction, death, metabolism, irritability, growth and differentiation, a heredity, an environmental adaptation and adjustment. The chapter by W. C. Allee, entitled "Social Dominance and Subordination Among Vertebrates," points to the fact that the dominance-subordination social pattern may be based on heredity, the physiologic state of the individual and psychological factors. A closer reciprocal understanding between the social and the biologic sciences is urged by I. Alfred E. Emerson in his chapter "Basic Comparisons: Human and Insect Societies," to the end that scientists shall not overlook the place of emotional force and emotion even in science. C. R. Carpenter gives an interesting and illuminating discussion on societies of monkeys and apes. In "The Societies of Primitive Man," A. L. Kroeber attempts to show that some measure of kinship of primitive man persists into higher civilization because kinship is biologically inescapable and perhaps equally inescapable psychologically. The concluding chapter "Modern Society," is by Dr. Robert E. Park, who discusses the "great society" from the distinguishing characteristics of size, complexity, speed, mechanism and freedom.

It seems to the reviewer that a careful reading of this instructive volume will give the reader a fair measure of intellectual balance in any further consideration of biologic phenomena.

Starling's Principles of Human Physiology. Edited and revised by C. Lovatt Evans, D.Sc., F.R.C.P., F.R.S., LL.D. With chapters on the special senses revised by H. H. H. ridge, M.D., Sc.D., F.R.S. Eighth edition. 8°, cloth, 121 pp., with 673 illustrations. Philadelphia: Lea and Febiger, 1941. \$10.00.

The author succeeds well in maintaining a proper balance in presenting the subject matter of physiology and its more important recent developments. The order adopted is in keeping with the courses given at University College. In this edition, the section covering the central nervous system has been entirely rewritten to conform to the newer knowledge in this field. The chapter on reproduction has been extensively revised, and a good deal of new matter has been added. The discussions on the endocrine organs, the vitamins and the urinary system and those sections concerned with biochemistry have been rewritten and rearranged. One will find many newly introduced figures of great teaching value. Although the book is essentially planned for the use of the student, the clinician can turn to it with considerable profit.

Boston City Hospital, and physician-in-chief, Waltham Hospital. 8°, cloth, 114 pp., with 11 charts. New York: The Commonwealth Fund, 1943. \$1.50.

This small work discusses the spectacular reduction in mortality due to some of the common diseases and seeks to ascertain the underlying causes of this decline.

Diagnosis of Uterine Cancer by the Vaginal Smear. By George N. Papanicolaou, M.D., Ph.D., Department of Anatomy, Cornell University Medical College; and Herbert F. Traut, M.D., Department of Obstetrics and Gynecology, Cornell University Medical College and the New York Hospital. 4°, cloth, 46 pp., with 11 color plates. New York: The Commonwealth Fund, 1943. \$5.00.

This volume describes a new, simple and inexpensive aid in the diagnosis of cancer of the uterus. The study is based on three years' experience in the Woman's Clinic at Cornell University.

Clinical Parasitology. By Charles F. Craig, M.D., M.A. (hon.), colonel, United States Army (retired); and Ernest C. Faust, M.A., Ph.D., professor of parasitology, Department of Tropical Medicine, Tulane University of Louisiana, consultant on tropical medicine and on epidemic diseases to the Secretary of War and to the United States Public Health Service. 8°, cloth, 767 pp., with 284 illustrations and 4 colored plates. Philadelphia: Lea and Febiger, 1943. \$9.00.

This new edition of a standard work has been brought up to date and new material relating to epidemiology in the field of human parasitology and on diseases transmitted to man by arthropods has been included. Four full-page color plates, two clinical tables and forty new figures have been added to the text. The table on the important malaria-transmitting mosquitoes of the world has been revised by Lt. Col. Paul F. Russell, Division of Preventive Medicine, Office of the Surgeon-General, Army of the United States. This work should prove valuable to medical and sanitary officers stationed in the tropics and the Orient.

Nutrition in Health and Disease. By Lena F. Cooper, B.S., M.A., M.H.E., chief, Department of Nutrition, Montefiore Hospital, New York City, dean, School of Home Economics, Battle Creek College, and supervising dietitian, United States Army (1918-1919); Edith M. Barber, B.S., M.S., editor of food column, New York *Sun*, and lecturer on history of cookery, Teachers College, Columbia University; and Helen S. Mitchell, B.A., Ph.D., chief nutritionist, Office of Foreign Relief and Rehabilitation Operations, State Department, and research professor in nutrition, Massachusetts State College. Ninth edition, revised. 8°, cloth, 716 pp., with 99 illustrations and 7 colored plates. Philadelphia: J. B. Lippincott Company, 1943. \$3.50.

This standard work on nutrition for use in schools of nursing has been thoroughly revised and brought up to date. Much new material has been added on the vitamins and a new chapter on food and nutrition problems in wartime. The table on the composition of foods has been revised and includes niacin, pyridoxine, pantothenic acid and biotin. A new feature of this edition is a glossary giving the concise definition of technical words and their pronunciation.

Gastro-Enterology. By Henry L. Bockus, M.D., professor of gastroenterology, University of Pennsylvania Graduate School of Medicine. Philadelphia: J. B. Lippincott Company, 1943. \$12.00.

stomach. 4°, cloth, 831 pp., with 134 illustrations, 21 tables. Philadelphia and London: W. B. S. Company, 1943. \$12.00.

This is the first volume of a system of diseases digestive tract and organs. The second volume, covering the small and large intestines, and the third volume covering the liver, biliary tract, pancreas and second intestinal disorders, will be published later. The purpose of the work is to include a discussion of every case and affection of the digestive tract. The author drawn on his large experience in the Gastrointestinal of the Graduate Hospital of the University of Penn

The Modern Treatment of Syphilis. By Joseph E. M.D., associate professor of medicine and adjunct professor of public-health administration, Johns Hopkins University, physician-in-charge, Syphilis Division, Clinic, and visiting physician, Johns Hopkins Hospital, Baltimore, and special consultant, United States Health Service. With the collaboration of Harold E. M.D.; Harry Eagle, M.D., surgeon, United States Health Service, and lecturer in medicine, Johns Hopkins University; Paul Paget, M.D., associate in medicine, Johns Hopkins University; Mary S. Goodwin, M.D., instructor in pediatrics, Johns Hopkins University; Frank W. Reynolds, M.D., instructor in medicine, Johns Hopkins University. Second edition; second 4°, cloth, 717 pp., with 109 illustrations and 12 Springfield, Illinois. Charles C Thomas, 1943. \$5.00.

This authoritative work was first published in 1931 and the second edition in 1941. The second edition is completely revised to the extent that twenty-three original thirty-two chapters of the first edition are completely rewritten and the other nine chapters extensively changed. The entire second edition is set from new type. A new chapter on the public aspects of the treatment of syphilis and a much discussion of infections in syphilis and its relation to the general health have been added. The bibliography has been brought about the same length as that in the first edition. The omission of older references to make room for the more recent ones. The second printing of the second edition has made possible the inclusion of a new chapter on venereal-disease control in the Army and Navy. In addition, the chapter on intensive arsenotherapy in syphilis has been thoroughly rewritten and brought up to date.

The Boy Sex Offender and His Later Career. By J. Doshay, M.D., Ph.D., psychiatrist, Children's Hospital, New York City. With a foreword by George W. M.D., associate professor of clinical psychiatry, University Medical College, consulting psychiatrist, Department of Correction, New York City, and consulting psychiatrist, New York Hospital. 8°, cloth, 206 pp., with 40 tables. New York: Grune & Stratton, 1943. \$3.00.

The author of this book has extensively reviewed over ten years examining thousands of patients in the clinics of the C's, the vitamins in New York City. His comments and conclusions are based on a relatively large number of cases. The book gives new lights on certain phases of juvenile sex delinquency. A rather startling conclusion is that the so-called "sex delinquents" are just as many a violent offender as the confirmed delinquents.

